Stroke Review
Advances in Interventional Neuroradiology 2004

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The year 2004 in interventional neuroradiology has been distinguished by the steady accumulation of evidence to validate the efficacy of therapeutic procedures, such as carotid angioplasty and stenting (CAS) for cerebrovascular atherosclerosis. There is increasing momentum to design trials that will validate the role of endovascular therapy in the treatment of acute stroke and other cerebrovascular disorders. Practice patterns continue to evolve as evidence-based principles are applied to interventional therapy.

Carotid Stenting
In September 2004, the US Food and Drug Administration approved the use of stents for the treatment of atherosclerotic disease of the carotid bifurcation. This approval was based on data from the industry-supported Acculink for Revascularization of Carotids in High Risk patients (ARChEr) registry and the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial. ARChEr showed a 10% complication rate for CAS in 581 high-risk patients compared with a 15% complication rate derived from the carotid endarterectomy (CEA) literature. SAPPHIRE was a randomized control trial (RCT) comparing CAS to CEA in 334 high-risk patients. Primary end points were the cumulative incidence of death, stroke, or myocardial infarction within 30 days and death or ipsilateral stroke between 31 days and 1 year. The overall rate of primary end points was 39% lower in the CAS group, and CAS resulted in complication rates for all adverse events ≤ CEA in both symptomatic and asymptomatic patients. The authors believe they have proven their hypothesis that CAS with distal protection is not inferior to CEA in high-risk patients. Criticisms of the study include the large proportion of asymptomatic patients, bias favoring CAS due to unequal randomization, the inclusion of many patients with recurrent stenoses after prior CEA, small sample size, and controversial end points, such as myocardial infarction and cranial nerve palsy. The evidence is also gathering that distal embolic-protection devices are essential to minimize complications in CAS. The Carotid Revascularization Endarterectomy versus Stent Trial (CREST) in North America is accelerating enrollment, and there are at least 3 European RCTs underway comparing CAS to CEA. The Asymptomatic Carotid Surgery Trial (ACST) showed that immediate CEA in asymptomatic patients <75 years of age with >70% stenosis halved the 5-year stroke rate from 12% with medical therapy to 6% (assuming a 3.1% surgical risk). Although similar to results of prior studies, this will undoubtedly fuel the trend toward treatment of asymptomatic disease with CAS. Despite the mounting evidence, there is still no long-term data on CAS to rival that of CEA, particularly in symptomatic patients who are not at high surgical risk.

Stenting of Intracranial Disease
Dedicated flexible cerebrovascular stents are now available to treat intracranial atherosclerotic stenoses, and 2 studies showed that this could be successfully performed in >95% of cases with complication rates <10%. Symptomatic restenosis, however, occurs in up to 67%, particularly with vertebral artery ostial lesions. The development of drug-eluting stents may address this problem. This procedure remains relatively high risk and requires careful patient selection.

Stroke
Mechanical devices for clot removal in acute stroke are becoming more sophisticated, and Phase I of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) Trial evaluated results in 28 patients treated within 6 hours of stroke onset. The device, a combination of microcatheter, retriever, and balloon catheter, was able to reopen 12 (43%) occluded arteries alone and 6 more (64%) with additional intra-arterial (IA) recombinant tissue plasminogen activator (rtPA). There was, however, a high incidence of intracranial hemorrhage (43%), although all were asymptomatic. Overall, 9 of the 18 patients (50%) with vessel recanalization had significant clinical recovery, compared with none of the 10 patients who showed no recanalization. Preliminary results from Phase II show that the therapeutic window can be extended to 8 hours, and in the 114 patients studied, successful recanalization was obtained in 53.5%, with a serious
procedural complication rate of 3.5%.12 Clot fragmentation based on laser technology (endovascular photoacoustic recanalization) has also been applied in 34 acute stroke patients.13 The overall recanalization rate was 41% with a 5.9% symptomatic hemorrhage rate and only 1 serious procedure-related complication. The combination of IV and IA rtPA remains intuitively attractive to facilitate rapid delivery of thrombolytic agents, and the Interventional Management of Stroke (IMS) Study14 showed that this strategy is feasible, but the results in 80 patients treated within 3 hours of the event showed little significant improvement in outcome compared with the placebo and treatment groups of the NINDS trial.15 IMS II is already underway and will also evaluate the use of a low-intensity ultrasound system (EKOS MicroLys). An RCT of IV/IA versus standard IV therapy is being planned.

Aneurysms

Technological developments continue for the treatment of wide-necked and complex cerebral aneurysms. Experience is accumulating with use of the Neuroform (Boston Scientific/Target) device for stent-assisted coiling of these lesions,16,17,18 and although occlusion rates can be improved, there are still significant problems with thrombo-embolic complications (up to 10%) and deployment difficulties. The stents are expensive, and there is no conclusive evidence for superiority over the balloon remodeling techniques employed successfully in Europe and elsewhere for many years. Covered stents are being developed for both intracranial and extracranial use.19 Promising new coil designs include those with a synthetic polymeric hydrogel coating to improve aneurysm packing density20 and a variable detachable system21 to minimize instrumentation inside the aneurysm lumen. The use of Onyx remains popular in Europe,22 but concerns about aneurysm recanalization (10% by 1 year) have resulted in waning interest in this technique in North America. As devices for cerebrovascular therapy become more complex and potentially thrombogenic, a better understanding and manipulation of the coagulation system is mandatory to prevent thrombo-embolic complications.23 There is ongoing debate about the impact of the International Subarachnoid Aneurysm Trial (ISAT)24 and pleas for more rigorous scientific evaluation of new coils and devices rather than simple reliance on case series, registries, and manufacturers claims.25

Arteriovenous Malformations

The techniques of endovascular therapy of cerebral arteriovenous malformations (AVMs) have changed little in the last few years, but the efficacy and the indications for these procedures are coming under increasing scrutiny. Although relatively high rates for complete AVM obliteration (22%) with n-butyl cyanoacrylate continue to be reported,26 preoperative or preradiosurgical embolization remain the primary therapeutic strategies. In a large series of 339 preoperative procedures,27 there was an 11% risk of death or permanent neurological deficit from the interventional therapy alone, with poor angiographic results in almost 8% of patients. There is a perception that the procedure may be overutilized in the US and that the benefits of decreased operative blood loss and normal perfusion breakthrough bleeding may only be realized in complex lesions, and that the risks do not justify use in more surgically straightforward AVMs.28 In another series of 118 patients, 88% of whom had undergone prior embolization, radiosurgery resulted in a 77% 5-year cure rate with an annual risk of adverse event rate (hemorrhage or stroke) of 3.9%.29 There is still no evidence that palliative embolization alone confers any benefit to patients, and partial embolization may actually increase the risk of hemorrhage.28 A retrospective analysis of 398 patients with unruptured brain AVMs (290 surgery and/or endovascular, 108 untreated) followed for an average of almost 5 years showed an annual bleeding rate of only 1.5% in the untreated patients, and that therapy resulted in a hemorrhage rate equal to that of untreated patients but with higher morbidity.30 The quest goes on to better understand the genetic background of this disease and to use this knowledge to improve and individualize treatments.31

Vasospasm

Post-hemorrhagic vasospasm continues to challenge those who treat cerebral aneurysms, and there is conflicting evidence as to whether there is any relationship of vasospasm severity to surgical clipping or endovascular coiling.32,33 The efficacy of traditional “Triple-H” therapy has been questioned,34 and old techniques such as multiple IA papaverine infusions have been revisited with some success.35 IA nimodipine36 and nicardipine37 have shown promise in small numbers of patients. Transdermal nitropaste38 and shunting of hemorrhagic cerebrospinal fluid through lumbar drains39 have been shown to reduce the degree of vasospasm and to improve outcome scores. Balloon angioplasty, however, remains the cornerstone of interventional management despite the risks of vessel dissection and rupture. Although conventional digital subtraction angiography (DSA) is the gold standard for diagnosing vasospasm, computed tomographic angiography (CTA) and CT perfusion techniques are becoming popular, less invasive screening alternatives.40,41

Imaging Advances

Rotational 3D DSA is now a standard feature of neuroangiographic units, and “3D roadmap” functionality may soon be available to extract the most information from imaging data sets to help guide interventional procedures.42 Improvements in X-ray detector technology may soon allow simultaneous CT cross-sectional imaging from angiographic units. Three-dimensional computational fluid dynamics will help us understand why aneurysms recanalize, enlarge, and rupture after interventional treatment.43 There is increasing reliance on the less invasive modalities to diagnose disease, plan treatment, and to predict therapeutic response. An evidence-based analysis of procedures used for the diagnosis of carotid stenosis44 showed that duplex ultrasound is the most cost-effective stand alone investigation for carotid stenosis, and that the addition of magnetic resonance angiography led to a marginal increase in quality-adjusted life-years gained but at a prohibitive cost. Duplex ultrasound with quantitative computer-assisted indices for carotid plaque analysis can predict the likelihood of distal embolization and neurological complications from CAS.45 DSA is being replaced by CTA as the sole...
diagnostic procedure before cerebral aneurysm therapy in some centers.46

References


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