Carotid artery stenting (CAS) has not been shown to be as safe as carotid endarterectomy for treatment of symptomatic extracranial carotid artery stenosis in the immediate postoperative period. However, beyond the postoperative period, data continues to support a role for CAS in selected patients. A large systematic review of 206 individual studies (54,713 total patients) undergoing CAS found the cumulative 30-day risk of stroke or death to be 7.6% in symptomatic and 3.3% in asymptomatic patients. Factors associated with increased risk of adverse outcomes in both groups were age >75 years (relative risk [RR] 1.88), hypertension (RR 1.86), and coronary artery disease (RR 1.41). Use of embolic protection devices significantly reduced the risk of stroke or death (RR 0.57). Although reports of adverse events vary widely in the literature, there has been a trend toward overall reduction in risk over the past several years, suggesting that use of embolic protection devices, careful patient selection, and increasing operator experience may be important factors in minimizing risk. The vast majority of these data (97%) are outside the standards of a randomized controlled trial (RCT), emphasizing the need for data from the trials that are currently enrolling patients. Among the larger studies currently enrolling patients are the Carotid Stenting for High Risk Surgical Patients (CHOICE, Abbott Vascular, target 5000 patients), Asymptomatic Carotid Surgery Trial-2 (ACST-2, target 5000 patients), and Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis versus Endarterectomy trial (SPACE-2, target 3640 patients).

This year, we received our first update from the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST), the largest RCT to date comparing the periprocedural safety and long-term (4 years) efficacy of CAS versus carotid endarterectomy. Data from the lead-in phase demonstrated an overall 30-day stroke and death rate of 4.4%. Restenosis rates in the lead-in phase were reported to be 13% with 1.2% of patients requiring repeat revascularization by 1-year follow-up. These numbers compare to restenosis rates of 10.7% and 4.6% in patients undergoing CAS and carotid endarterectomy, respectively, in the SPACE trial and 19% of CAS patients in the Stenting and Angioplasty with Protection in Patients at High Risk of Endarterectomy (SAPPHIRE) study. The Carotid Revascularization Using Endarterectomy or Stenting Systems (CаRESS) trial, a prospective, nonrandomized comparative cohort study reported no difference in rates of death, nonfatal stroke, and myocardial infarction (MI) at 4 years postprocedure (27% versus 22%, carotid endarterectomy versus CAS, P=0.27). However, consistent with data from other studies, restenosis rates were higher in the CAS group (P=0.014). Thirty-day results from 4007 patients enrolled in the SAPPHIRE trial were published demonstrating a 4.4% rate of all MI, stroke, and death.

Still one of the most intriguing and controversial subjects is that of CAS in octogenarians. A single-center retrospective study of 24 octogenarians undergoing CAS reported a 30-day morbidity and mortality of 4.2%. Prospectively acquired data pooled from 3 centers demonstrated no difference in 30-day rates of death, transient ischemic attack, or MI between 2 cohorts selected by age (mean age 69.9 and 83.5 years, respectively). Touze et al, however, pooled data from 22 individual studies (14,184 patients >75 years of age) and found that patients in the older subgroup had a RR of 1.88 (P<0.01) for death, MI, and stroke. These conflicting findings again emphasize the need for large randomized cohorts including patients of advanced age. The cumulative data suggest that excellent outcomes are viable with CAS performed by seasoned experts in selected patients.

Intracranial Artery Angioplasty and Stenting
Management of symptomatic intracranial atherosclerotic disease (ICAD) remains controversial. One of the largest retrospective single-center studies to date of 111 patients demonstrated no difference in favorable outcome (symptom resolution, no new ischemic events, and modified Rankin Scale [mRS] score of $\leq 3$) between optimal medical therapy (antiplatelet agents, statins, risk factor modification) and angioplasty and stenting for treatment of symptomatic intracranial atherosclerotic disease. Data continues to accumulate demonstrating high restenosis rates (up to 50%) in the poststenoterm period using the Wingspan stent. Furthermore, there appears to be a subset of target lesions that are refractory to multiple treatments. In comparison, a large single-center study of 113 patients treated with balloon-mounted stents demonstrated stroke or transient ischemic attack in 6.74% and a restenosis rate of 20% during the follow-up period of 29±16 months. Diabetes and hyperlipidemia were associated with the incidence of restenosis. As we await the results of the randomized multicenter National Institutes of Health (NIH)-funded trial on the use of the...
Wingspan stent (Boston Scientific) for the treatment of ICAD (stenting versus aggressive medical management for preventing recurrent stroke in intracranial stenosis) and the VISSIT trial (Vitesse Intracranial Stent Study for Ischemic Therapy, Micrus Endovascular, see illustrative case in the Figure), we have a systematic review pooled data from 31 studies (1177 procedures) using angioplasty and stenting for treatment of symptomatic, high-grade intracranial artery stenosis. High initial rates of technical success were offset by variable rates of periprocedural adverse events (minor and major stroke, death, 0% to 50%). Complication rates were higher in the posterior versus anterior circulation (12.1%, versus 6.6%, P<0.01), and restenosis rates (>50%) were higher using self-expanding stents versus balloon-mounted stents (17.4 versus 13.8, P<0.001). However, the lack of standardized treatment protocols, study designs, and imaging techniques limits interpretation of these studies. It was therefore under careful consideration that standardization protocols for interventional treatment of ICAD were developed this year to enable comparison among comparable data sets in the future. Until the RCT data emerges, angioplasty and stenting for treatment of symptomatic ICAD should be preferentially performed on carefully selected patients in high-volume centers.

Acute Ischemic Stroke

Devices and techniques for the interventional treatment of acute ischemic stroke (AIS) are evolving rapidly, making the execution of large RCTs difficult as the enrollment periods often far exceed the technology development cycle. Large trials sponsored by National Institute of Neurological Disorders and Stroke (NINDS), both the Interventional Management of Stroke-III (IMSIII) and MR and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE), are cognizant of this point and have been revised to include newer device technology that have achieved FDA approval. The community awaits the data from these large RCTs, but in the interim we rely on a lower level of evidence to guide interventional treatment of AIS. This year in the stroke literature, we continued to learn about existing techniques and
have been excited about new technologies, in particular the growing body of evidence to support the use of self-expanding stents for revascularization.

One of the oldest yet simplest techniques in the neuroendovascular armamentarium has been the local delivery of thrombolysis through a microcatheter placed near the occlusive thrombus (IA thrombolysis). A single-center, prospective, nonrandomized registry demonstrated that the combination of a bridging dose of IV tissue plasminogen activator (tPA) (0.6 mg/kg) and IA tPA (0.3 mg/kg) with adjuvant mechanical procedures if needed (snare or balloon angioplasty) led to an 87% recanalization rate in 53 patients, as evidenced by imaging or transcranial Doppler 24 hours after treatment.16 The control arm that received full dose IV tPA (107 patients) had significantly less recanalization (52%). Functional recovery at 90 days (mRS 0–2) was 57% in the combined IA-IV group as compared to 44% in the IV group, which was not statistically different. Interestingly, clinical outcome was correlated to both recanalization and time to recanalization; however, perhaps the enrollment was too small to realize improvement in functional outcome with the combined IA-IV therapy. Unlike the Emergency Management of Stroke Bridging Trial, mortality was the same in both groups and the IA-IV group experienced less symptomatic intracranial hemorrhage (European Cooperative Acute Stroke Study criteria) than the IV only group (9% versus 11%). In direct contradiction, the MR Stroke Study Group reported in their retrospective analysis of 645 patients that receiving IA delivery of a lytic with or without adjunctive IV tPA was an independent predictor of increased rates of symptomatic intracranial hemorrhage versus IV tPA (odds ratio [OR] 3.4, 95% CI 1.2 to 10.0, P<0.05). The analysis of a small number of patients receiving IA lytic (n=74) or IA-IV treatment (n=35) was hindered by variations of the IA thrombolysis protocol. Nonetheless, the investigators guess that high concentrations of thrombolytic drugs delivered locally to an intracranial vessel may lead to augmented activation of proteases at the blood–brain barrier.

Experience and data analysis of mechanical embolectomy for AIS treatment has expanded in 2009. One of the largest criticisms of the revolutionary Mechanical Embolectomy in Acute Ischemic Stroke trials (MERCI and Multi-MERCI) was that the 90-day mortality was higher than the control arm of the Prolyse in Acute Cerebral Thromboembolism II trial (PROACT II), which was the historic control that evaluated IA thrombolysis with recombinant prourokinase. However, because the MERCI trials were not limited to middle cerebral artery occlusions and in the end enrolled older patients with a more severe baseline stroke score than PROACT II, comparisons between the trials cannot be made. This year the Merci and Multi Merci investigators parsed their data for patients who would have been eligible for enrollment in PROACT II.18 They were able to conclude that mortality was indeed explained by baseline stroke characteristics and trial design, and did not differ between the relevant patients in the MERCI trials and PROACT II control arm. Moreover, embolectomy produced similar functional outcome results in this subset of MERCI/multi-MERCI patients as compared to the PROACT II treatment arm. It is important to mention that adjusted comparisons were hampered by the failure to obtain access to the individual patient level data from PROACT II.

The results of the Penumbra Pivotal Stroke Trial were in print in 2009.19 As reported at the International Stroke Conference last year, this new aspiration device has a very high rate of “target vessel” recanalization (defined as thrombolysis in myocardial infarction [TIMI], 2 to 3 at the site of primary occlusion). Encouraging are the target vessel recanalization rate (>80%) and safety (<3% procedural serious adverse event) associated with the use of the Penumbra aspiration system. The rate of symptomatic intracranial hemorrhage (11.2%) trended higher than the MERCI trials, but deemed acceptable in light of the aforementioned benefits. However, the functional outcome (mRS 0–2 at 90 days) was surprisingly low at 25% (29% in patients with successful recanalization), bringing into question the role of recanalization in positive functional recovery. In our initial laboratory and clinical experience with this device (unpublished, 2009), we have confirmed its ease of use and excellent periprocedural safety profile; however, frequent clot fragmentation with distal embolization was observed. This is often managed with the use of smaller Penumbra devices to aspirate the fragments or adjunctive IA thrombolysis. It appears that the real world, posttrial experience and implementation of the aforesaid techniques is demonstrating higher functional recovery rates around 45% in patients recanalized with the Penumbra devices.20 It is important to note that the initial high recanalization rates as well as excellent safety profile continue to be confirmed.20–22

Continuing from last year’s Advances in Interventional Neuroradiology,23 perhaps the most exciting development in 2009 regarding the endovascular treatment of AIS was the use of self-expanding stents for flow restoration. The use of stents in AIS refractory to other endovascular treatments was applied in 2 small, retrospective series this year and achieved between 92% to 100% recanalization rates.24,25 The first prospective FDA approved trial, Stent-Assisted Recanalization in Acute Ischemic Stroke, demonstrated in 20 patients a 100% recanalization rate,26 defined as TIMI 2 to 3 flow evidenced by arteriography. There was only 1 (5%) symptomatic hemorrhage and 1 month mRS was 0 or 1 in 45% of the treated patients. The disadvantage of this approach is the implantation of a permanent vascular prosthesis and the necessity of dual-antiplatelet therapy. Using the advantages of the stent-in-stroke concept along with unique solutions, such as temporary stent-bypass with a retrievable device,27 may provide an optimal interventional treatment.

The role of imaging in patient selection for interventional treatment of AIS advanced in 2009.28 Additionally, we were updated at the annual meeting of the Society of Neurointerventional Surgery on the progress of the DWI and CTP Assessment in the Triage of Wake-up and Late Presenting Strokes Undergoing Neurointervention (the DAWN Trial).29 These data strongly suggested that excellent functional outcome can be achieved via aggressive intraarterial revascularization in patients with viable penumbra as determined by CT or MR imaging at a mean of 16 hours from last seen well. In the report, 193 AIS patients received intervention at a mean of 16.3 hours after the last time they were seen well, and good
functional outcome (mRS ≤2) after 90 days was recorded in 46% of the patients. Symptomatic intracerebral hemorrhage and mortality in this group were 10% and 22%, respectively. Statistically significant predictors of good functional outcome were age (OR 0.96, 95% CI 0.93 to 0.99), time to treatment (OR 1.11, 95% CI 1.01 to 1.21), and successful recanalization (OR 3.21, 95% CI 1.21 to 8.51). These data suggested not only that patients can be successfully treated at much later time points than most prior studies have permitted, but also that proper patient selection by penumbral imaging at all time points may improve functional neurological outcomes. At this juncture, the latter point is still controversial requiring further study.

Aneurysms

In 2009 we had another update from the International Subarachnoid Aneurysm Trial (ISAT),39 a large RCT designed to compare clinical outcomes for patients having ruptured aneurysms treated by endovascular coiling or surgical clipping. The 5-year clinical data established decreased mortality in the endovascular group versus the surgical group (OR 0.75, 95% CI 0.58 to 0.97, P = 0.03). These latest data with more than 8000 person-years of follow-up in each arm demonstrated that 1.2% and 0.4% of aneurysms treated by coiling and clipping rebled after the first year, respectively (intent-to-treat analysis, P = 0.06). Although late rebleeding has been shown to be higher in the endovascular treatment arm as compared to the surgery group by the actual treatment received, the risk remained small and there was no difference in death related to rebleeding between the treatment groups.

Another multicenter, non–RCT in which 1036 aneurysms in 929 patients were treated with bare embolic coils was available in 2009.31 Of the 804 patients with ruptured aneurysms, the risk of rebleeding up to 10 years after coiling was 0.6%. In both ruptured and unruptured aneurysms, the retreatment rate was 6%. In a single-center experience that followed 270 patients over a mean period of 22 months after receiving coil embolization for ruptured aneurysms, 2.1% of these aneurysms rebled.32 Most rehemorrhages in this study occurred within 30 days of coiling and rebleeding was significantly associated with initial incomplete coil embolization. In a systematic literature review of studies reporting data on endovascular aneurysm treatment, it was found in a largest series to date (142 aneurysms) reported 2.8% morbidity and 2% mortality associated with use of latest neurovascular stent technology. For over a decade, balloon-remodeling technique has been used as a simple measure to embolize wide-neck brain aneurysms. The Analysis of Treatment by Endovascular approach of Nonruptured Aneurysms (ATENA), a multicenter nonrandomized prospective study, sought to compare the risks associated with the balloon-assisted coiling (n = 222) as compared to traditional coil embolization (n = 325).40 There were no differences in procedural-related complications, permanent morbidity, or mortality between the groups. These data support the concept that balloon-assisted coil embolization is a safe technique; however, the question remains that whether this approach, which is often used for wide-neck complex aneurysms, will provide durable coil embolization. In a single-center study limited to aneurysm embolization of 114 middle cerebral artery aneurysms, complex anatomy requiring the use of balloon-remodeling was significantly related to recanalization.43

The growing experience to use low-profile, microcatheter-delivered, self-expanding stents continued to generate enormous excitement. The hope remained that stent-assisted coil embolization (SAC) may improve long-term durability of the endovascular approach.41-42 A recent single-center experience in 107 wide-neck aneurysms in which SAC was performed showed that the procedure-related morbidity and mortality was 5.6 and 0.9%, respectively. The authors reported that favorable clinical outcome (mRS score 0 to 2) was achieved in 90.7% of the patients after a mean of 47 months. Angiography performed in nearly half of the patients after a mean of 37 months demonstrated a recanalization rate of 13.7%. The largest series to date (142 aneurysms) reported 2.8% morbidity and 2% mortality associated with use of latest neurovascular stent technology.44 We continue to await follow-up data from this multicenter study to see whether the presence of the stent will reduce recanalization rates. An outstanding question remained regarding the use of SAC in acutely ruptured aneurysms, because the deployment of these devices requires antiplatelet therapy that is disadvantageous in the setting of subarachnoid hemorrhage. A multicenter, nonrandomized study in Finland reported their experience in using SAC in 61 patients with ruptured aneurysms.45 The technical success rate was 72% and complications related to SAC occurred in 21%. The majority of complications were the result of thromboembolism. Over a mean follow-up period of 1 year, 69% of the patients had a good outcome, meaning the Glasgow outcome scores were 4 or 5. SAC in the setting of acutely ruptured aneurysms requires more extensive study at...
this point and is not recommended outside the setting of a RCT.

Before the FDA approval of the Guglielmi Detachable Coil, researchers were already exploring the concept of flow diversion for the treatment of brain aneurysms. Essentially, the concept incorporated 2 phenomena, namely, the disruption of the fluid momentum transfer into the aneurysm sac and the scaffold that produces a remodeling effect of the vascular wall with neointimal growth. The embodiment today of this concept is low-porosity braided stents. The Pipeline braided stent (eV3 Neurovascular), and other stent-like devices and stent grafts have potential to represent a paradigm shift in the treatment of intracranial aneurysms away from coil embolization and toward parent vessel reconstruction and flow diversion as well as vessel-preserving strategy for vascular wall lesions. Published preliminary results in human aneurysms were extremely encouraging. At 6- and 12-month follow-up, obliteration rates attained from flow diversion exceeded 90% in 28 and 18 patients, respectively. In an era of healthcare reform, we learned this year that although endovascular treatment of aneurysms has shorter hospitalization, surgical clipping of these lesions is associated with lower costs. This result was attributed to the high cost of materials (ie, embolic coils) in the endovascular group. The replacement of numerous coils deposited within the aneurysm sac by a single-flow diversion device may offer not only a superior strategy in terms of patient safety and aneurysm obliteration, but also an economical solution. Two clinical trials have commenced to seek the approval of the Pipeline device in the United States.

In conclusion, these data presented in 2009 continued to cement the role of endovascular treatment of brain aneurysms. One large unanswered question is when to use this treatment in unruptured aneurysms? Because patients with unruptured intracranial aneurysms had never been the subjects of a randomized trial, the Trial on Endovascular Aneurysm Management (TEAM) began enrolling patients with unruptured intracranial aneurysms to compare the combined morbidity and mortality of endovascular treatment with conservative management over a projected 10-year period of follow-up. Unfortunately, low enrollment in the TEAM trial led to its announced cancellation at the 2009 Congress of the World Federation of Interventional Therapeutic Neuroradiology. Undeterred, researchers sought markers to detect the rupture risk of unruptured aneurysms. Aneurysm wall inflammation was correlated with ruptured aneurysms and preliminary research indicates that intraaneurysmal inflammation can be imaged noninvasively. Further development of these techniques may lead to quantitative assays to assess the risk of rupture in unruptured brain aneurysms that could improve patient selection for endovascular treatment.

Arteriovenous Malformations
A single-center investigation of n-butyl-2-cyanoacrylate (nBCA) embolization in 202 brain arteriovenous malformations (bAVMs) became available this year. Permanent morbidity as a result of embolization was 2.5% over a mean follow-up period of 43 months. Using these data from 377 embolization procedures, the investigators were able to devise a new grading system that may prognosticate embolization risks with nBCA. Embolization with the relatively new material, ethylene-vinyl alcohol (Onyx, eV3 Neurovascular), was further investigated this year. This nonadhesive polymer injected in solution with an organic solvent (dimethyl sulfoxide, DMSO) that evaporates leading to Onyx precipitation, was approved by the US FDA in 2005 for embolization of bAVMs. French investigators reported their prospective multicenter study of Onyx in 50 bAVMs during 116 embolization sessions. An additional 33 sessions involved nBCA. After 1 month, the morbidity and mortality of the embolization was 8% and 2%, respectively. More than 60% occlusion of the bAVMs by volume was attained in 73% of the cases. Two retrospective single-center studies reported a median reduction in bAVM volume of 75% following Onyx embolization in 123 patients with periprocedural morbidity rates from 12.2 to 19.5%. The reported obliteration rates by Onyx embolization alone ranged from 8% to 24%–54–56; however, one study found a 50% recanalization rate. A histopathologic analysis of excised bAVMs was published in 2009 that allowed for detailed comparisons between embolization with nBCA (n=10) and Onyx (n=22). Histology revealed vascular or perivascular inflammation in 90% of cases in both groups. Both foreign body giant cell infiltration and recanalization were seen in Onyx embolized vessels and not in the nBCA group. This result might have been impacted by the time difference from embolization to surgical resection, which was 8 and 18 days in the nBCA and Onyx groups, respectively. Although the authors reported deeper penetration of the Onyx material into the bAVM nidus as compared to nBCA, these data are strongly related to both material properties and technique. Therefore, this result requires validation in a multicenter study. Onyx definitely has expanded the endovascular approach to bAVMs; however, increased complete obliteration rates harbor higher risk of bleeding, which is likely the result of venous outflow obstruction. We expect that as experience with Onyx grows proper selection of bAVMs for and techniques of Onyx embolization will lead to decreased complications.

Disclosures
None.

References


10. Deleted in proof.


KEY WORDS: carotid artery ■ neuroradiology ■ advances