Cerebrovascular Surgery Update

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Key words: subarachnoid hemorrhage, aneurysm, arteriovenous malformation, intracerebral hemorrhage, ischemic stroke

Introduction

The field of cerebrovascular surgery has always been dynamic since its establishment. We will cover four main subtopics, aneurysms, arteriovenous malformations (AVMs), intracerebral hemorrhage (ICH), and ischemic stroke.

Aneurysms

I. Unruptured aneurysms

Clinical equipoise exists between treatment and no treatment for anterior circulation aneurysms between 5 to 10 mm and posterior circulation aneurysms between 3 and 10 mm. A recent study has found that the surgical treatment of unruptured aneurysms reduces mortality when compared to the natural history of the disease. The risk of hemorrhage during surgery was 4% and the risk of hemorrhage after surgery was 0.1% per year (50% of these were due to untreated or new aneurysms). Overall, only 0.5% of the patients died from a subsequent subarachnoid hemorrhage (SAH) over an 8.5-year average follow up. However, the authors have suggested a 10-year follow up. Patients under the age of 50 years with non-giant anterior circulation aneurysms do better with surgery than either coiling or conservative management.

Advances in neuroimaging techniques have dramatically changed the diagnosis of cerebral aneurysms. Noninvasive angiographic methods, such as computed tomography (CT) angiography and magnetic resonance (MR) angiography, allow for detection and characterization of aneurysms, further enhanced by postprocessing techniques that enable three-dimensional (3D) evaluation of aneurysm morphology. Contemporaneous parenchymal imaging with CT or MR imaging yields a wealth of information that may assist surgical planning. CT angiography may detect aneurysms greater than 1–2 mm, providing detailed evaluation of morphology such as relationship to the parent vessel and neck width. CT angiography can detect more than 95% of aneurysms identified on conventional angiography. CT angiography may be superior to MR angiography because of shorter acquisition times, diminished motion artifacts, and detailed demonstration of other landmarks. However, bone and venous structures may complicate analysis. Once diagnosed, newer modalities like computational flow dynamics coupled with 3D CT/digital subtraction angiography (DSA)/MR angiography are now found to predict the risk of rupture of an aneurysm based on the flow characteristics of the aneurysm.

Various factors affect the treatment decision. The important ones predicting increased risk of rupture and thus indicating treatment are age of the patient (more than 10 years of life expectancy), aneurysm size (more than 3 mm), aneurysm location (posterior circulation), aneurysm morphology (larger aspect ratio, irregular morphology, daughter aneurysms, blebs, higher non-sphericity index), previous history of SAH, clinical presentation (related to mass effect, transient ischemic attacks [TIAs], newly developed symptoms), and positive family history (family members with histories of aneurysmal SAH) (Fig. 1). Asymptomatic cavernous carotid aneurysms may be safely observed, as the risk of rupture is low and rupture will not cause SAH, but instead result in cavernous-carotid fistulas. Internal carotid artery aneurysms, vertebrobasilar artery aneurysms, aneurysms with well defined neck <4 mm, and aneurysms with no efferent vascular branches from the base are all suitable for endovascular treatment. Other aneurysms require surgical clipping. There have been no randomized comparisons of coiling versus clipping for unruptured aneurysms.

The treatment of aneurysms (both surgical and endovascular) is becoming more and more safe, so including more and more unruptured aneurysms suitable for treatment as the risk of observation exceeds that of treatment. Most of the mortality is related to the associated co-morbidities like atherosclerosis,
cardiac ischemia, etc.

II. Ruptured aneurysms

SAH incidence varies greatly between countries, from 2 cases/100,000 in China to 22.5/100,000 in Finland. Community-based studies reported an incidence that ranged from 8.1 per 100,000 in Australia and New Zealand to 23 per 100,000 in Japan. Many cases (64% in 1985 to ~12% recently) of SAH are misdiagnosed. Risk factors for SAH include hypertension, smoking, female sex, and heavy alcohol use. Cocaine-related SAH occurs in younger patients, with outcome similar to that in other SAH patients. Familial intracranial aneurysm syndrome occurs when two first- through third-degree relatives have intracranial aneurysms. Importance of recognition of a warning or sentinel leak cannot be overemphasized. A high index of suspicion is warranted. The diagnostic sensitivity of CT is not 100%, so diagnostic lumbar puncture should be performed if the initial CT is negative. Good quality CT will detect SAH in more than 95% of the cases, if done within 48 hours of the ictus. In the first 12 hours after SAH, the sensitivity of CT for SAH is 98% to 100%, declining to 93% at 24 hours and to 57% to 85% 6 days after SAH. MR imaging is not sensitive within the first 24–48 hours (because of the very low methemoglobin), but may be helpful after 4–7 days in the case of subacute to remote SAH (>10–20 days), and in detecting which of the aneurysms bled in the patients with multiple aneurysms or if CT has been negative for SAH, when the fluid-attenuated inversion recovery sequence of MR imaging may prove to be more sensitive.

Cerebral angiography is the gold standard for visualization of the aneurysm, but many centers have reported good results with CT angiography with the advantage of 3D reconstruction and surrounding bone configuration, ease, and speed. Sensitivity is 95% and specificity 83% for detecting aneurysms as small as 2.2 mm. Catheter angiography is not an innocuous procedure, with rates of 1.8% for ischemic neurological deficits (transient or permanent), and 1–2% for rerupture. If CT indicates anterior circulation aneurysm rupture, but aneurysms cannot be identified, it is important to visualize the flow contrast through the anterior communicating artery, even using cross carotid compression if required, before declaring that the angiogram as negative. Similarly, if CT is compatible with posterior circulation aneurysm bleed, both posterior inferior cerebellar artery origins must be visualized, even if both vertebral arteries must be catheterized.

The severity of the initial bleed should be determined rapidly as it is the most useful indicator of outcome following aneurysmal SAH, and grading scales which heavily rely on this factor are helpful in planning future care with family and other physicians. On admission, the first problem is to find any treatable causes of altered sensorium or focal neurological deficits (like large intracerebral hematoma), which should be immediately resolved. After survival through the initial hours of SAH, the next step is to prevent the main neurological complications, rebleeding, delayed brain ischemia, hydrocephalus, seizures, and hyponatremia.

Up to 14% of SAH patients may experience rebleeding within 2 hours of the initial hemorrhage. Case review and prospective cohorts have shown that for untreated, ruptured aneurysms, there is at least a 3% to 4% risk of re-bleeding in the first 24 hours and possibly significantly higher, with a high percentage occurring immediately (within 2 to 12 hours) after the initial ictus, a 1% to 2% per day risk in the first month, and a long-term risk of 3% per year after 3 months, with a cumulative risk of 40%. After rebleeding the prognosis is poor, 80% of patients die or remain disabled. Unfortunately not many factors have been identified that predict increased risk of bleeding, but include the severity of initial bleeding, interval to admission, blood pressure, sex, aneurysm characteristics, hydrocephalus, early angiography, and the presence of ventricular drainage. Urgent evaluation and treatment of patients with suspected SAH is therefore recommended. Re-bleeding was more common in those with a systolic blood pressure >160 mmHg. Blood pressure should be monitored and controlled to balance the risk of strokes, hypertension-related rebleeding, and maintenance of cerebral perfusion pressure. Anti-fibrinolytic therapy may reduce rebleeding but has not been shown to improve out-
comes, but may be considered in certain clinical situations, such as patients with a low risk of vasospasm and/or a beneficial effect of delaying surgery. Recent evidence suggests that early treatment with a short course of antifibrinolytic agents combined with a program of early aneurysm treatment followed by discontinuation of the antifibrinolytic agent and prophylaxis against hypovolemia and vasospasm may be reasonable.\(^{36}\)

Isolation of the aneurysm from the normal circulation is the most effective step to prevent rebleeding, and can be achieved by surgical methods (clipping) or endovascular methods (coil embolization). Endovascular occlusion of the aneurysms with intraluminal coils is mainly reserved for patients with poor condition, posterior circulation aneurysms, and elevated surgical risk. Coil embolization is associated with a 2.4% risk of aneurysm perforation and an 8.5% risk of ischemic complications. The International Subarachnoid Aneurysm Trial reported a 1-year re-hemorrhage rate of 2.9% in aneurysms treated with endovascular therapy. Post-treatment SAH occurred at an annualized rate of 0.9% with surgical clipping, compared to 2.9% with endovascular treatment. The rate of incomplete obliteration and recurrence appears significantly lower with surgical clipping than with endovascular treatment. Individual characteristics of the patient and the aneurysm must be considered in deciding the best means of repair, and management of patients in centers offering both techniques is probably recommended. Surgical clipping or endovascular coiling is strongly recommended to reduce the rate of rebleeding after aneurysmal SAH. Wrapped or coated aneurysms as well as incompletely clipped or coiled aneurysms have an increased risk of rebleeding compared to completely occluded aneurysms and therefore require long-term follow-up angiography. Complete obliteration of the aneurysm is recommended whenever possible.\(^{42}\)

Increased time to treatment is associated with increased rates of preoperative re-bleeding at 0 to 3 days, 5.7%; 4 to 6 days, 9.4%; 7 to 10 days, 12.7%; 11 to 14 days, 13.9%; and 15 to 32 days, 21.5%, whereas postoperative re-bleeding did not differ among time intervals (1.6% overall).\(^{37}\) Although previous studies showed that overall outcome was not different for early versus delayed surgery after SAH, early aneurysm treatment is reasonable and is probably indicated in the majority of cases, as early treatment reduces the risk of rebleeding after SAH, and newer methods may increase the effectiveness of early aneurysm treatment.

The preoperative neurological status of the patient, which is determined by the severity of the initial hemorrhage, is a major determinant of endovascular or surgical treatment of ruptured aneurysms.\(^{38,39}\) Estimating the consequences of complications attributable to an operation may be possible from data regarding surgery for unruptured aneurysms, for which the in-hospital mortality rates vary from 1.8% to 3.0% in large multicenter studies\(^{5,40,41,57}\) and adverse outcomes in survivors vary from 8.9% to 22.4%. Although previous studies showed that overall outcome was not different for early versus delayed surgery after SAH, early treatment reduces the risk of rebleeding after SAH, and newer methods may increase the effectiveness of early aneurysm treatment. Early aneurysm treatment is reasonable and is probably indicated in the majority of cases.\(^{42}\)

Treatment volume is an important determinant of outcome for intracranial aneurysms—higher volume equals lower mortality.\(^{43–46}\) This effect may be more important for patients with unruptured aneurysms than for those with ruptured aneurysms, but whether the benefits of receiving care at a high-volume center would outweigh the costs and risks of transfer remain uncertain.\(^{43}\)

Treatment of cerebral vasospasm begins with early management of the ruptured aneurysm, and maintaining normal circulating blood volume and avoiding hypovolemia is probably indicated.\(^{47}\) Two small single-center prospective randomized studies strongly suggest that avoiding hypovolemia is advisable, but there is no evidence for prophylactic hypervolemic-hemodilution therapy depending on the clinical scenario. Calcium-channel blockers, particularly nimodipine, have been approved for use for treatment of vasospasm, but the reduction in morbidity and improvement in functional outcome may be more due to cerebral protection than the actual effect on the cerebral vasculature.\(^{50,51}\) Intravenous nicardipine interestingly showed a 30% reduction in spasm but no improvement in outcome.\(^{52}\) Balloon angioplasty has been shown to be effective in reversing cerebral vasospasm in large proximal conducting vessels but has not been shown to improve ultimate outcome and is not effective or safe in distal perforating branches beyond second-order segments.\(^{53,54,56}\) It is effective in reducing angiographic spasm, promoting increase in cerebral blood flow, and reducing deficits, but carries the risks of vessel occlusion, vessel rupture, thrombus formation, and aneurysm clip displacement.\(^{58,59,82}\)

Acute hydrocephalus, which occurs in 20–30% of
SAH cases,60–63) is more frequent in patients with poor clinical grade and higher Fischer scale scores.34,65) Two single-center series suggested that routine fenestration of the lamina terminalis reduces the incidence of chronic hydrocephalus. Temporary or permanent cerebrospinal fluid diversion is recommended in symptomatic patients with chronic hydrocephalus following SAH.

Retrospective reviews report that early seizures occur in 6% to 18% of SAH patients,64,66,67) most commonly in the first 24 hours,68) and more commonly in SAH associated with ICH, hypertension, and middle cerebral artery (MCA) and anterior communicating artery aneurysms.69) Delayed (mean 18 days after SAH) non-convulsive seizures (recorded on electroencephalography) have been reported to occur in 19% of stuporous or comatose SAH patients.70) The administration of prophylactic anticonvulsants may be considered in the immediate post-hemorrhagic period. The routine long-term use of anticonvulsants is not recommended but may be considered for patients with risk factors such as prior seizure, parenchymal hematoma, infarct, or MCA aneurysms.

Hyponatremia occurs in 10–30% of SAH patients and is more common in patients with poor clinical grade, anterior communication artery aneurysms, and hydrocephalus, and may be an independent risk factor for poor outcome.71–74) Administration of large volumes of hypotonic fluids and intravascular volume contraction should generally be avoided following SAH to avoid hyponatremia, and once developed, the use of fludrocortisone acetate,18,75) hypertonic saline,77) and 5% albumin76) is reasonable for correction.

AVMs

I. Unruptured AVMs

Whatever the treatment technique, the crude proportion of treatment-associated morbidity usually ranges around 10% in the most recent reports, but this seems acceptable given the persistent risk of potentially devastating bleeding from an untreated AVM. Current natural history data from the Columbia AVM Database, the University of California San Francisco AVM Study project, and the Scottish Intracranial Vascular Malformation Study suggest the annual risk of spontaneous hemorrhage may be as low as 1% for unruptured AVMs. In addition, the growing availability of MR imaging has led to a substantial increase in the incidental detection of unruptured malformations ranging between 54% and 62% of all diagnosed AVMs in modern population-based data sets. In the light of these figures, neurovascular teams face the clinical dilemma of how to balance the inherent risk of intervention against the potentially low hemorrhage rates in patients harboring an unruptured brain AVM. These figures raise concern that invasive treatment may be connected with an unfavorable benefit vs. risk ratio to the degree that some have become reluctant to recommend interventional therapy for many patients presenting with unruptured AVM. Evidence-based guidelines give nonintervention as one option in AVM management. Although current clinical practice favors intervention in most patients, some clinicians understandably prefer to undertake intervention in specific subgroups of patients who are likely to benefit from the intervention. Besides hemorrhagic presentation, predictors of AVM hemorrhage during natural history follow-up include increasing age, deep brain location, associated aneurysms, and exclusive deep venous drainage. In contrast, the risk of spontaneous hemorrhage may drop below 1% per year in AVMs without these risk factors. These characteristics may guide the neurovascular team during case assessment and patient counseling, but the fact that the same factors not only increase the natural history risk but also the hazard of intervention, clearly adds to the complexity. Careful explanation and sufficient time must be given to the patients, because they are often otherwise healthy young adults who are actively involved in their working and family life.

Although data from randomized trials to guide the choice of treatment are lacking, surgical resection, radiosurgery, embolization, or combinations are appropriate for grade I to III AVMs. The choice of treatment will depend on the specific features of the lesion, with consideration of the age of the patient, presence or absence of bleeding and associated aneurysm, diameter and location of associated aneurysms, and pattern of venous drainage. Surgery is recommended for grade I and II AVMs,80) and consideration of endovascular embolization followed by microsurgery is recommended for grade III. However, the long-assumed benefit of interventional therapy seems to have become less clear in the management of unruptured AVMs. Consideration of radiosurgery is recommended for lesions that may be associated with an increased risk of surgical complications, owing to their anatomical location or feeding vessel anatomy, in particular for lesions in the eloquent area. Palliative treatment is suggested for grade IV and V AVMs with intranidal or arterial aneurysms or progressive neurological deficits related to vascular steal. Complete treatment is recommended for patients with progressive neurological deficits caused by hemorrhage of the AVM. Grade
IV and V lesions are generally not treated because of the risks of treatment, under the American Stroke Association (ASA) recommendation 2001.

The absence of randomized studies on AVM treatment leads to considerable uncertainty in the existing clinical literature on indications for invasive treatment in these patients. The best way to address the issue is a randomized clinical trial. The currently launched Randomized Trial of Unruptured Brain AVMs (ARUBA) is a randomized, multicenter, international trial comparing the outcome of invasive treatment with conservative management in patients with unbled AVMs. A potential solution to the clinical dilemma posed by an unruptured brain AVM is randomization in the ARUBA (www.arubastudy.org). ARUBA is investigating treatment for consenting adults aged ≥18 years, with an unruptured brain AVM that is potentially treatable, over a minimum follow-up period of 5 years, based on outcome assessments by physicians. The intention is to compare the long-term outcomes for two groups of patients over a period of at least 5 years. To date 102 centers across U.S.A., U.K., and Australia have enrolled. We will have to wait for fresh data from this study to enhance our knowledge on management of unruptured AVMs. Until the ARUBA study results are available (2012), treatment is recommended for younger patients with one or more of the high risk features for an AVM rupture, whereas an older individual or a patient with no high risk features may be best treated by managing only the medical aspects, such as anticonvulsants for seizure control and appropriate analgesia for headaches.

II. Ruptured AVMs

Recent studies have suggested that the majority of brain AVMs are now diagnosed as unruptured lesions, and that the risk according to natural history among these lesions may be less than previously assumed. Even so, AVMs represent the most common cause of isolated, nontraumatic ICH in young adults. The most important factors governing the operability of an AVM are location, size, age of the patient, and the neurosurgeon’s experience. The best and definitive treatment of cerebral AVMs still remains complete microsurgical removal in experienced hands. However, microsurgical technique of complicated AVMs remains one of the most difficult tasks of microsurgery: unlike tumor surgery, incomplete removal will lead to death or disability.

CT with angiography followed by DSA can establish the diagnosis. DSA is the gold standard and can provide dynamic data on the angio-architecture, real size, and location of AVM. In small AVMs with large hematomas treated as emergencies, CT angiography may be adequate and less time consuming. MR imaging helps better understanding of the AVM site and anatomy, and functional MR imaging and tractography are helpful in AVMs located in eloquent areas.

Preoperative Onyx embolization has brought a revolution in treating large AVMs, as many of these can, after extensive filling with Onyx, be occluded and/or resected without difficulties. However, complete obliteration of an AVM by regular embolization is rare (10%), but with slowly setting glue (Onyx) even up to 50% of the selected cases can be totally occluded.

Surgical extirpation is strongly suggested as the primary treatment for Spetzler-Martin grade I and II AVMs if surgically accessible with low risk. Radiation therapy is recommended for Spetzler-Martin grade I or II AVMs if less than 3 cm in size and surgery has an increased surgical risk based on location and vascular anatomy. Brain AVM of Spetzler-Martin grades III can often be treated by a multimodal approach with embolization followed by surgical extirpation. If the lesion has a high surgical risk based on location and vascular anatomy, radiation therapy may be performed after embolization. Spetzler-Martin grade IV and V AVMs are often not amenable to surgical treatment because of the high procedural risk. These AVMs can be approached by a combined multimodal approach of embolization, radiosurgery, and/or surgery. In general, embolization should only be performed if the goal is complete AVM eradication with other treatment modalities. The only exception is palliative embolization in patients with Spetzler-Martin grade IV or V AVM with venous outflow obstruction or true steal phenomenon in order to reduce arterial inflow to control edema or to reduce the amount of shunt, respectively.

The goal of embolization is to block the high velocity shunting of blood from the high pressure arterial system into the venous system. Serial embolization sessions may whittle the AVM down to a fraction of its original size; the reduced AVM size and the presence of embolic material within the AVM make surgery and radiosurgery safer and more accurate. Embolization may be intended to produce relief of neurological symptoms caused by a large lesion, even if the goal of treatment is not complete obliteration. In most cases, only embolization is not sufficient to completely obliterate the AVM. However, isolated case series have reported 11–40% of AVM obliteration with only endovascular embolization.

Radiosurgery is an option to treat AVMs that are approximately 3 cm in diameter or less. Proton
beam, linear accelerator, or gamma knife methods are used to deliver a high dosage of radiation to the AVM, while minimizing the effects to surrounding brain tissue; a single dose generally is given. Proton beam irradiation sometimes is attempted with larger lesions. Radiotherapy is thought to work by inducing thrombosis. This approach is appealing because of its apparent noninvasiveness. MR imaging often shows hyperintensity in the surrounding brain white matter following treatment; actual mass effect from edema can be seen when larger territories are covered. Radiosurgery may take 1–3 years to achieve thrombosis of an AVM, so the patient remains at risk for hemorrhage from the AVM during the treatment period.

Trials directly comparing treatment approaches are lacking, and information on outcomes derives largely from case series. Complete obliteration is the goal of treatment as partial obliteration does not affect the rate of hemorrhage.

III. Aneurysms associated with AVM

Aneurysms on an artery that does not feed the AVM can be managed as any unruptured intracranial aneurysm. Aneurysms of less than 5 mm in size have been reported to regress after treatment of AVM; in other cases, they have ruptured after treatment. Given the concern about aneurysms greater than 5 mm, treatment via microsurgical clipping or endovascular coiling is generally performed prior to the treatment of the AVM.

Stroke

Disturbances in cerebral perfusion are due to ischemia in 80–83% of cases, to ICH in 10–12%, and to SAH in the remaining 7–8%. Two-thirds occur in the territory of the anterior circulation, and may arise from embolization from the heart, extracranial or intracranial large vessels, or intracerebral microvascularity. Not all are related to atherosclerosis, as some are caused by arterial dissection. Incidence of stroke is 600–800 per 100,000 persons per year in the 65–74 year old age group, with higher incidence in Japan, Finland, and Scotland.

I. Ischemic stroke

Emergent CT is indicated to rule out hemorrhage, early signs of ischemia, and especially if anticoagulation or thrombolytic therapy is considered or if surgical lesion is suspected indicating an emergency carotid endarterectomy (CEA). However, CT is normal in the first 12–24 hours in 8–69% of ischemic non-lacunar MCA cerebrovascular accidents. MR imaging is more sensitive than CT, especially between 8 and 24 hours post ictus, and more importantly in brainstem and cerebellar infarction.

A large number of stroke trials were performed during the last decade, but the only 2 successful intravenous stroke thrombolysis trials were part 1 and part 2 of the National Institute of Neurological Disorders and Stroke (NINDS) recombinant tissue plasminogen activator (rtPA) trials. These resulted in Food and Drug Administration approval of intravenous thrombolysis with rtPA for the treatment of ischemic stroke in selected patients within 3 hours after stroke onset. This is now considered worldwide as “standard of care.”

Intra-arterial thrombolysis is typically considered when patients miss the therapeutic 3-hour window for intravenous thrombolysis. The intra-arterial approach has been promoted because a high concentration of thrombolytic agents may be delivered into the cerebral circulation at the location of the occlusive thrombus in conjunction with mechanical clot manipulation or extraction. Mechanical revascularization may be beneficial in occluded cerebral arteries with a large clot burden. Intra-arterial thrombolysis has been tested only in a few controlled trials.

Recently, a case-control study was reported from Japan Multicenter Stroke Investigator’s Collaboration. Clinical outcomes for 91 patients who presented within 4.5 hours after stroke onset and received intraarterial urokinase were compared with a matched control group of 182 patients who did not receive intra-arterial urokinase. The modified Rankin scale score at discharge was significantly lower in the urokinase group than in the control group (2.8 versus 3.3, respectively). A favorable outcome (modified Rankin scale scores of 0 to 2) was observed more frequently in the urokinase group (51%) than in the control group (34%). Recanalization rates for major cerebrovascular occlusions with the intra-arterial therapy approach were 70% compared with 34% with intravenous thrombolysis, and especially most apparent in patients with internal carotid artery, carotid terminus, or proximal MCA occlusions.

The American Heart Association/ASA guidelines for the early management of adults with ischemic stroke concluded that intra-arterial thrombolysis is an option for the treatment of selected patients who have major stroke of 6-hour duration due to occlusions of the MCA who are not otherwise candidates for intravenous rtPA. Interventional Management of Stroke (IMS) I and II trials showed that complete recanalization was achieved within 120 minutes in 68.9% of patients with the EKOS Primo catheter (EKOS Corp, Bothell, Wash., U.S.A.) with sonography activation.
compared with 53.3% of patients by use of either the EKOS Primo catheter without sonography activation or IMS I microcatheter intervention. Successful revascularization was correlated with good outcome. IMS III trial is now under way to test combined intravenous and intra-arterial thrombolytic therapy along with intra-arterial appliances such as the EKOS microinfusion catheter and the Concentric Merci thrombectomy device (Concentric Medical, Inc., Mountain View, Calif., U.S.A.).

Intra-arterial thrombolysis is also reasonable for patients who have contraindications to the use of intravenous thrombolysis, such as recent surgery. The availability of intra-arterial thrombolysis should generally not preclude the intravenous administration of rtPA in otherwise eligible patients. Treatment requires the patient to be at an experienced stroke center with immediate access to cerebral angiography and qualified interventionalists. Facilities should define criteria to credential individuals who can perform intra-arterial thrombolysis. There is increased risk of symptomatic ICH with the use of rtPA (NIHSD study: 6.4% vs. 0.6% with placebo; European Cooperative Acute Stroke Study II: 8.8% vs. 3.4%). The factors associated with increased risk of symptomatic ICH are severity of National Institutes of Health Stroke Scale score, or pretreatment CT showing brain edema or mass effect.

The Concentric Merci device can be useful for extraction of intra-arterial thrombi in appropriately selected patients, but the utility of the device in improving outcomes after stroke remains unclear. The usefulness of other endovascular devices is not yet established, but may be beneficial. A recent trial of mechanical clot extraction with the Penumbra System® (Penumbra, Inc., San Leandro, Calif., U.S.A.), a device designed to revascularize large vessel occlusions in the intracranial circulation, was completed recently, and publication in a peer-reviewed journal is pending.

Decompressive craniectomy may reduce the mortality associated with MCA infarct with severe cerebral edema from 37% to 32% in the non-dominant hemisphere, with reduction in hemiplegia. Better results are achieved with early surgery.

Cardiogenic brain embolism is the only condition for which anticoagulation has been shown to significantly prevent the rate of further cardiovascular accidents. Twelve percent of patients with cardiogenic pulmonary embolism will have recurrent embolism within the next 2 weeks, and this risk must be weighed against the risk of converting the pale infarct into the hemorrhagic infarct before starting anticoagulation.

II. Spontaneous ICH

ICH causes 10% to 15% of first strokes, with a 30-day mortality rate of 35% to 52%; half of the deaths occur in the first 2 days. The recent dramatic increase in clinical trials of ICH/intraventricular hemorrhage and the initial findings from these trials provide great hope for new and effective treatments for patients with ICH.

CT and MR imaging are both first choice initial imaging options; in patients with contraindications to MR imaging, CT should be obtained. MR imaging is also superior to CT for the identification of associated vascular malformations, especially cavernoma. However, MR imaging is not as practical as CT for all presenting patients.

Monitoring and management of patients with ICH should take place in an intensive care unit setting because of the severity of the condition, frequent elevations in intracranial pressure and blood pressure, frequent need for intubation and assisted ventilation, and multiple complicating medical issues. Appropriate antiepileptic therapy should always be used for treatment of clinical seizures in patients with ICH. Early mobilization and rehabilitation are recommended in patients with ICH who are clinically stable. Treatment with recombinant activated clotting factor VII within the first 3 to 4 hours after onset to slow progression of bleeding has shown promise in one moderately sized phase II trial; however, the efficacy and safety of this treatment must be confirmed in phase III trials before use in patients with ICH can be recommended outside a clinical trial.

The Surgical Trial in Intracerebral Haemorrhage compared “early” surgery with initial conservative treatment for 1033 patients with ICH. The average time from the onset of symptoms to surgery was 30 hours (range 16 to 49 hours), and the average time for only 16% (74 of 465 patients) was fewer than 12 hours. At 6 months, good functional outcome was seen in 26% (n = 122) for the surgical group, which was not significant compared to 24% for the medical group (odds ratio 0.89, 95% confidence interval 0.66 to 1.19). The absolute 2.3% (3.2% to 7.7%) and relative 10% (13% to 7.7%) benefits for early surgery over initial conservative medical treatment were also found to be nonsignificant.

Patients with cerebellar hemorrhage > 3 cm who are deteriorating neurologically or have brain stem compression and/or hydrocephalus from ventricular obstruction should undergo surgical removal of the hemorrhage as soon as possible. Although stereotactic infusion of urokinase into the clot cavity within 72 hours of ictus apparently reduces the clot burden and risk of death, rebleeding is more common, and
functional outcome is not improved; therefore, its usefulness is unknown. Although theoretically attractive, the usefulness of minimally invasive clot evacuation utilizing various mechanical devices and/or endoscopy awaits further testing in clinical trials; so the current usefulness is unknown. For patients presenting with lobar clots within 1 cm of the surface, evacuation of supratentorial ICH by standard craniotomy might be considered. The routine evacuation of supratentorial ICH by standard craniotomy within 96 hours of ictus is not recommended, with the possible exception of patients with lobar clots within 1 cm of the surface as above.

No clear evidence at present indicates that ultra-early craniotomy improves functional outcome or mortality rate. Operative removal within 12 hours, particularly when performed by less invasive methods, has the most supportive evidence, but the number of subjects treated within this window is very small. Very early craniotomy may be associated with increased risk of recurrent bleeding. Delayed evacuation by craniotomy appears to offer little if any benefit with a fairly high degree of certainty. In patients presenting in coma with deep hemorrhages, removal of ICH by craniotomy may actually worsen outcome and is not recommended. Too few data currently exist to comment on the potential of decompressive craniectomy to improve outcome in ICH.

III. Occlusive cerebrovascular disease

For patients with recent TIA or ischemic stroke within the last 6 months and ipsilateral severe (70% to 99%) carotid artery stenosis, CEA is recommended performed by a surgeon with a perioperative morbidity and mortality of <6% (Class I, Level of Evidence A). For patients with recent TIA or ischemic stroke and ipsilateral moderate (50% to 69%) carotid stenosis, CEA is recommended, depending on patient-specific factors such as age, sex, comorbidities, and severity of initial symptoms. If the degree of stenosis is <50%, there is no indication for CEA. When CEA is indicated for patients with TIA or stroke, surgery within 2 weeks is suggested rather than delaying surgery. Among patients with symptomatic severe stenosis (>70%) which is difficult to access surgically, medical conditions may be present that greatly increase the risk for surgery, or other specific circumstances exist such as radiation-induced stenosis or restenosis after CEA, so carotid artery stenting is not inferior to endarterectomy and may be considered. Carotid artery stenting can be indicated if performed by operators with established periprocedural morbidity and mortality rates of 4% to 6%, similar to that observed in trials of CEA and carotid artery stenting. Among patients with symptomatic carotid occlusion, extracranial-intracranial bypass surgery is not routinely recommended.

Endovascular treatment of patients with symptomatic extracranial vertebral artery stenosis may be considered if symptoms persist despite medical therapies (antithrombotics, statins, and other treatments for risk factors). The usefulness of endovascular therapy (angioplasty and/or stent placement) is uncertain for patients with hemodynamically significant intracranial stenoses who have persistent symptoms despite medical therapies (antithrombotics, statins, and other treatments for risk factors) and is considered investigational.

For patients with noncardioembolic ischemic stroke or TIA, antiplatelet agents rather than oral anticoagulation are recommended to reduce the risk of recurrent stroke and other cardiovascular events. Aspirin (50 to 325 mg/dl), combination of aspirin and extended release dipyridamole, and clopidogrel are all acceptable options for initial therapy. For patients with ischemic stroke or TIA and extracranial arterial dissection, use of warfarin for 3 to 6 months or antiplatelet agents is acceptable. Beyond 3 to 6 months, long-term antiplatelet therapy is reasonable for most stroke or TIA patients. Anticoagulant therapy beyond 3 to 6 months may be considered for patients with recurrent ischemic events. For patients with definite recurrent ischemic events despite adequate antithrombotic therapy, endovascular therapy (stenting) may be considered. Patients who fail or are not candidates for endovascular therapy may be considered for surgical treatment.

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