AHA Scientific Statement

Indications for the Performance of Intracranial Endovascular Neurointerventional Procedures

A Scientific Statement From the American Heart Association Council on Cardiovascular Radiology and Intervention, Stroke Council, Council on Cardiovascular Surgery and Anesthesia, Interdisciplinary Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research

Philip M. Meyers, MD, FAHA, Chair; H. Christian Schumacher, MD, Co-Chair; Randall T. Higashida, MD, FAHA, Co-Chair; Stanley L. Barnwell, MD, PhD; Mark A. Creager, MD, FAHA; Rishi Gupta, MD; Cameron G. McDougall, MD; Dilip K. Pandey, MD; David Sacks, MD; Lawrence R. Wechsler, MD, FAHA

Intracranial endovascular cerebrovascular interventions treat cerebrovascular diseases by use of minimally invasive intravascular techniques. This area of expertise has made tremendous strides during the past decade, and the rate of progress has accelerated as the discipline has gained increasing clinical acceptance. An Accreditation Council for Graduate Medical Education–approved training curriculum has been developed and approved since 2000,[1,2] and an increasing body of clinical and scientific evidence demonstrates the application, safety, and efficacy of endovascular techniques for the treatment of cerebrovascular diseases. Several nonneurologically based endovascular subspecialties, such as vascular medicine, vascular surgery, and interventional cardiology, perform carotid artery stent placement with neurorescue via alternative Accreditation Council for Graduate Medical Education pathways, as well as a clinical practice pathway.[3]

Largely because of developments in computer-aided imaging and high-resolution digital subtraction angiography with reconstruction techniques, as well as easier access to the cerebral vasculature through improved microcatheter design, navigation of the cerebral and spinal vasculature is now de rigueur. Technological developments continue to occur rapidly. The purpose of the present document is to review the current information and data for the efficacy and safety of procedures used for intracranial endovascular interventional treatment of cerebrovascular diseases and to provide recommendations for their use based on the best available evidence. Table 1 shows the American College of Cardiology (ACC)/American Heart Association (AHA) classification of recommendations and levels of evidence. Moreover, the present document characterizes the expected success and complication rates for intracranial endovascular interventional procedures when performed by highly skilled operators. This information should be useful to enable assessment of the appropriateness, safety, and efficacy of neurovascular procedures for individual operators and institutional programs. A summary of the procedures discussed in this document, recommendations, and levels of evidence is provided in Table 2.

Writing Group Composition

The writing group was selected to represent a broad range of experience, perspective, and expertise on neurovascular disease and treatment. Participants were solicited from the AHA councils and interdisciplinary working groups by the AHA's chief scientific officer. The members of the writing group were identified on the basis of 1 or more of the following attributes: Neurointerventionalists with a broad range of experience (in practice and in academic settings); clinical researchers who study the outcome of neurovascular procedures and stroke; directors of neuroendovascular training and

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on January 30, 2009. A copy of the statement is available at http://www.americanheart.org/presenter.jhtml?identifier=3003999 by selecting either the "topic list" link or the "chronological list" link (No. LS-2038). To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

Expert peer review of AHA Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit http://www.americanheart.org/presenter.jhtml?identifier=3023366.

(*Circulation*. 2009;119:2235-2249.)

***Circulation* is available at http://circ.ahajournals.org** **DOI: 10.1161/CIRCULATIONAHA.109.192217**

Table 1. Applying Classification of Recommendations and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT ↓ / SIZE OF TREATMENT EFFECT →	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *Risk ≥ Benefit* Procedure/Treatment should **NOT** be performed/administered **SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations†	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

†In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All guideline recommendations have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendatins), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

treatment programs; and individuals knowledgeable about neurovascular diseases.

Literature Review

A computerized search of the National Library of Medicine database of literature (PubMed) from 1966 to July 2007 was conducted with 2 goals: (1) To identify published neurological and intracranial endovascular cerebrovascular interventional outcome data that could be used as benchmarks for quality assessment; in addition, the process sought to identify those risk-adjustment variables that affect the likelihood of success and complications. (2) To identify data that can be used as the basis for monitoring the appropriateness of performance of endovascular cerebrovascular procedures.

Broad keyword phrases for disease entities, including *cerebral aneurysm*, *stroke*, *arteriovenous malformation*, and *cerebral stenosis*, were used in conjunction with procedural terms, including *coil*, *stent*, *thrombolysis*, *intervention*, and *endovascular treatment*. Only English-language articles or articles with English-language translation were included. Abstracts were reviewed, and articles unrelated to the specific topic were excluded. Duplicate references and redundant publications were discarded. An analysis of treatment and outcome was performed according to the ACC/AHA classification of recommendations and level of evidence (Table 1).

Cerebral Aneurysms

Although cerebral aneurysms affect a relatively small number of Americans each year (incidence 6 to 16 per 100 000[4–7]; prevalence 0.5% to 6% of the population[8–10]), their importance is highlighted because of the severe morbidity and mortality associated with subarachnoid hemorrhage that re-

Table 2. Summary of Indications and Recommendations for Endovascular Procedures

	Indications	Recommendations	Recommendation Class and Level of Evidence
Cerebral aneurysm			
Ruptured with SAH	If amenable to endovascular treatment according to endovascular specialist	Should be considered for endovascular occlusion	Class I, LOE B
Unruptured	If amenable to endovascular treatment according to endovascular specialist	Reasonable to consider endovascular occlusion	Class IIa, LOE B
Intracranial atherosclerosis			
Symptomatic stenosis	For symptomatic atherosclerotic stenosis >70% failing medical therapy	May be reasonable to consider endovascular revascularization with angioplasty or stenting	Class IIb, LOE C
Acute ischemic stroke			
Intra-arterial thrombolysis	For patients with major stroke syndrome of <6 hours' duration and ineligible for intravenous thrombolysis	Reasonable to consider intra-arterial thrombolysis in selected patients	Class I, LOE B
Mechanical disruption	For patients with major stroke syndrome of <8 hours' duration and ineligible for or failing intravenous thrombolysis	May be reasonable to perform mechanical disruption to restore cerebral blood flow in selected patients	Class IIb, LOE B
Cerebral AVM			
Pial AVM	For patients with hemorrhage referable to the AVM, endovascular treatment in combination with other therapies such as surgery or radiosurgery	May be considered as a preoperative adjunct or palliative treatment in an effort to prevent recurrent hemorrhage	Class IIb, LOE C
Dural AV fistula	For patients with neurological symptoms or hemorrhage referable to the AVM, endovascular treatment alone may be curative or may be used in combination with other therapies such as surgery or radiosurgery	May be considered as a preoperative adjunct or palliative treatment in an effort to prevent stroke or hemorrhage	Class IIb, LOE C

SAH indicates subarachnoid hemorrhage; LOE, level of evidence; AVM, arteriovenous malformation.

sults from rupture of cerebral aneurysms. Three percent of all stroke cases are due to ruptured saccular aneurysms, but more than 5% of stroke deaths are due to aneurysmal hemorrhage, and more than 50% of these patients die within the first 30 days after the ictus.[7,11] In the 1960s, McKissock et al[12] demonstrated that the benefits of craniotomy and surgical clipping of cerebral aneurysms outweighed the risks without surgery, depending on the location of the aneurysm. Since that time, there have been advances in microsurgical techniques, such as the operating microscope; nevertheless, only a minority of subarachnoid hemorrhage victims survive without disabling neurological or cognitive deficits.[13]

In 1990, the Guglielmi Detachable Coil (GDC) was introduced into clinical use for the treatment of cerebral aneurysms.[14,15] Initially used as an experimental device, the GDC system (Boston Scientific, Freemont, Calif) received US Food and Drug Administration (FDA) approval in 1995 for the treatment of surgically unclippable aneurysms. Thereafter, endovascular occlusion of ruptured and unruptured cerebral aneurysms has proliferated throughout the world. There is an increasing array of coil technology available from a number of medical device companies to treat cerebral aneurysms. Second-generation biologically active coil technology intended to improve the efficacy and durability of endovascular treatment has become available recently, but its efficacy remains unproven. Liquid embolic agents to improve occlusion rates of aneurysms are being studied (Onyx Liquid Embolic System, Onyx HD-500, Micro Therapeutics, Inc, Irvine, Calif),[16] but their use has been limited to a few centers. Adjunctive techniques to aid coil occlusion of wide-neck aneurysms, such as balloon-remodeling and stent-assisted coil occlusion, have also been developed. In September 2002, the FDA approved the Neuroform stent (Boston Scientific), the first cerebrovascular stent device, to augment treatment of wide-necked cerebral aneurysms.[17,18] Newer, second-generation stents (Johnson and Johnson Cordis Neurovascular, Miami Lakes, Fla) that are now resheathable, ie, recaptured in the delivery system if not fully deployed with a closed cell design, have recently been introduced worldwide for use in aneurysms previously deemed difficult to treat by endovascular techniques.[19] Obliteration of aneurysms with stent technology is also currently being investigated in the treatment of giant aneurysms with the Pipeline stent (Chestnut Medical, Menlo Park, Calif)[20] and other similar devices.

Ruptured Cerebral Aneurysms

The International Subarachnoid Aneurysm Trial (ISAT) is the most comprehensive study to date that directly compared the safety and efficacy of endovascular coil occlusion with surgical clipping of ruptured cerebral aneurysms.[21,22] ISAT was a multicenter, prospective, randomized trial. Its primary objective was to determine whether endovascular coil treatment resulted in fewer dead or dependent patients, defined by a modified Rankin score of 3 to 6 at 1 year after the procedure. This study enrolled 2143 patients with an acute subarachnoid hemorrhage due to a ruptured intracranial cerebral aneurysm at 43 centers, predominantly in Europe,

Australia, and North America. Most patients (88%) randomized were in good neurological condition (World Federation of Neurosurgical Societies grades I or II), and most had small aneurysms (92% were less than 11 mm in diameter.) The primary criterion for enrollment of a patient was agreement between the neurosurgeon and the endovascular specialist that the patient's aneurysm could be treated by either method. Enrollment commenced in 1994 and was halted prematurely by the steering committee in April 2003 for ethical reasons when the Data Monitoring Committee determined that the primary end point had been reached.

ISAT showed that endovascular coil occlusion of cerebral aneurysms results in substantially better patient outcomes than neurosurgical clipping.[21] There was a relative risk reduction of 22.6% (95% confidence interval [CI] 8.9% to 34.2%) and an absolute risk reduction of 6.9% (95% CI 2.5% to 11.3%, $P=0.00082$) for death or disability at 1 year. The 1-year outcome measurement point was selected to include the effects of subsequent procedures that these patients may have required and also to detect any early rebleeding that could impair functional outcomes. The rebleeding rates were low in both the endovascular and surgical groups (2.4% and 1%, respectively) and were not considered to be significant; however, the rate of seizures was substantially lower in the endovascular group (relative risk 0.52, 95% CI 0.37 to 0.74).[22] The survival advantage in the endovascular group was maintained up to 7 years, with an absolute risk reduction of 7.4% (95% CI 3.6% to 11.2%, $P=0.03$).[22] Aneurysm retreatment occurred throughout the follow-up period in both the endovascular (17.4%) and neurosurgical clipping (3.8%) groups, but the likelihood for retreatment was 6.9 times higher in the endovascular group, thus requiring ongoing surveillance.[23] The Medical Research Council of Great Britain granted funding for ISAT through 2007 for additional data collection. These data were to include the cost-effectiveness of endovascular coiling versus surgical clipping, quality-of-life analysis, delayed angiographic findings, and rebleeding rates.

Despite global enthusiasm for the ISAT data, there have been a number of criticisms. The vast majority (78%) of patients potentially eligible for inclusion in ISAT were excluded. Nine percent of patients refused participation, whereas 69% were not deemed treatable either by the endovascular specialist or by the neurosurgeon who would perform the clipping. This left only 31% of patients who were deemed suitable for endovascular treatment, which is significantly lower than in many clinical practices. Because of disparities in time before the aneurysm was secured in the endovascular and surgical groups (longer time in the clipping group), more patients experienced rehemorrhage in the surgical group. Operator experience also may have biased the results, because the interventional neuroradiologists performing the coiling procedures were highly specialized, whereas the neurosurgeons predominantly practiced general neurosurgery, not specifically vascular neurosurgery. Finally, many aneurysms in the endovascular group were incompletely occluded compared with aneurysms clipped in the surgical cohort (66% versus 82%, respectively). Additional time will be necessary to determine the significance of incomplete aneurysm treatment.

The Cerebral Aneurysm Rerupture After Treatment (CARAT) study was designed to evaluate the risk of recurrent hemorrhage after endovascular aneurysm coil occlusion or surgical aneurysm clipping.[24] The trial included 1010 patients who were treated at 9 large medical centers in the United States from 1996 to 1998. Participants were identified by medical record review, then contacted by telephone or postal questionnaire. Maximum follow-up was 9.6 years (mean 4.4 years) for clipped aneurysms and 8.9 years (mean 3.7 years) for coiled aneurysms. Two hundred forty-one patients had died at the time of follow-up. Among the survivors, the rerupture risk for coiled aneurysms was 0.11% (95% CI 0% to 0.63%), whereas it was 0% (95% CI 0% to 0.14%) for clipped aneurysms.[24]

When both of these trials are taken into consideration, endovascular coiling appears to have better clinical and neurological outcomes. Ideally, patients should be managed in centers that offer both open surgical and endovascular techniques.

Recommendation

1. Endovascular coil occlusion of the aneurysm is appropriate for patients with a ruptured cerebral artery aneurysm that is deemed treatable either by endovascular coiling or by surgical clipping (*Class I, Level of Evidence B*).

Unruptured Cerebral Aneurysms

The natural history of unruptured aneurysms and the role of treatment are less clear. Consequently, the management of unruptured intracranial aneurysms remains controversial. Nevertheless, unruptured aneurysms are diagnosed with increasing frequency as cerebral imaging techniques improve and are applied more commonly. The International Study of Unruptured Intracranial Aneurysms (ISUIA) aimed to assess the natural history of unruptured aneurysms and to measure the risk associated with their treatment.[25] From 1991 to 1998, 4060 patients were prospectively enrolled and observed over a 5-year period; 1692 patients with 2686 aneurysms did not receive treatment, whereas 1917 patients underwent craniotomy and surgical clipping, and 451 received endovascular coil therapy.

ISUIA raises important concerns about the natural history of intracranial aneurysms and their treatment. Fifty-one patients (3%) in the untreated cohort experienced a subarachnoid hemorrhage during the study period. Nearly all hemorrhages occurred within 5 years of diagnosis, and the majority of ruptured aneurysms were at least 7 to 9 mm in diameter. For patients with aneurysms <7 mm in diameter in the anterior cerebral circulation, the risk of rupture was 0.1% per year. Yet, the range for the risk of hemorrhage was quite broad and was related to size and location. For instance, the risk of aneurysm rupture ranged from 0% to 40% depending on size in the anterior cerebral circulation and from 2.5% to 50% using the same size criteria in the posterior circulation and posterior communicating arteries.

Combined surgical morbidity and mortality at 1 year was 10.1% for patients without prior subarachnoid hemorrhage and 12.6% for patients with prior subarachnoid hemorrhage.

In the endovascular group, combined treatment morbidity and mortality at 1 year was 7.1% in patients without prior subarachnoid hemorrhage and 9.8% in patients with prior subarachnoid hemorrhage. Morbidity and mortality varied according to patient age, aneurysm size, and location. Young patients (less than 50 years of age) with asymptomatic aneurysms had the lowest surgical morbidity and mortality (5% to 6% at 1 year). Meanwhile, greater patient age did not affect the risk of aneurysmal hemorrhage but was associated with a higher risk of surgical morbidity and mortality.[25] Endovascular aneurysm treatment in patients older than 50 years was safer than craniotomy and surgical clipping but not statistically so. Because the endovascular treatment cohort (451 patients) was relatively small, wide CIs and substantial variance limit comparability with the surgical cohort.[25] Moreover, the study was neither randomized nor controlled, thus limiting its overall validity. Despite these limitations, ISUIA includes some of the best data available on the natural history of unruptured cerebral aneurysms and the effect of their treatment.

Other studies reported cohorts of patients with unruptured cerebral aneurysms retrospectively, comparing clinical outcomes between endovascular versus surgical morbidity. One of the largest of these reviewed 2535 treated, unruptured cerebral aneurysm cases.[26] These cases came from 429 hospitals in 18 states during a 1-year time period.[26] Metrics used in this study included effectiveness (as measured by hospital discharge outcomes that measured mortality rates), adverse outcomes (death or discharge to a rehabilitation or nursing facility), length of stay, and hospital charges. Endovascular treatment compared with neurosurgical treatment was associated with fewer adverse outcomes (6.6% versus 13.2%), decreased mortality (0.9% versus 2.5%), shorter lengths of stay (4.5 versus 7.4 days), and lower hospital charges ($42 044 versus $47 567; combined $P<0.05$). After multivariable adjustment, neurosurgical cases had 70% greater odds of an adverse outcome, 30% higher hospital charges, and 80% longer length of stay than endovascular cases ($P<0.05$). The authors concluded that endovascular therapy is associated with significantly less morbidity, less mortality, and decreased hospital resource use at discharge compared with conventional neurosurgical treatment for all unruptured aneurysms.[27] These data would require corroboration with a large, prospective, randomized study.

The Trial on Endovascular Aneurysm Management (TEAM) aims to study the safety and efficacy of endovascular treatment of cerebral aneurysms to prevent aneurysmal subarachnoid hemorrhage.[28] Funded by the Canadian Institutes of Health Research, the authors hope to recruit 2002 patients over a 3-year period, then monitor their clinical progress over a 10-year period. Because of controversy in the neurosurgical community, no surgical clipping group is being included in the study.

Recommendations

1. A number of factors should be considered to determine whether patients with unruptured cerebral aneurysms should receive conservative management with observation or intervention by surgical clipping or endovascular coil occlusion. These factors include the size of the cerebral aneurysm, a history of prior subarachnoid hemorrhage from any source, the age of the patient, family history of cerebral aneurysms, and multiple aneurysms or concurrent pathology of other cerebrovascular disorders, such as brain arteriovenous malformation,[29,30] fibromuscular dysplasia,[31] dissection,[32,33] cerebral arteritis,[34–39] or other conditions that may predispose to higher risk for hemorrhage (*Class IIb, Level of Evidence C*).
2. Patients with unruptured cerebral aneurysms who are considered for treatment should be fully informed about the risks and benefits of endovascular treatment as an alternative to surgical aneurysm clipping (*Class IIa, Level of Evidence B*). Endovascular coiling can be effective and is associated with a reduction in procedural morbidity and mortality over surgical clipping in selected cases (*Class IIa, Level of Evidence B*). Endovascular coiling is reasonable to consider as an alternative to surgical clipping in selected cases (*Class IIa, Level of Evidence B*).

Endovascular Cerebral Revascularization With Stent-Angioplasty

Intracranial atherosclerosis accounts for approximately 8% to 9% of all ischemic strokes in population-based or hospital-based studies. It is estimated that 40 000 to 60 000 strokes occur annually in the United States due to intracranial atherosclerosis.[40,41] In general, intracranial atherosclerosis occurs in the setting of widespread atherosclerosis. Asians,[42–44] blacks,[45] and Hispanics[46] are more likely to have intracranial atherosclerosis than whites. Besides race and ethnicity, risk factors associated with intracranial atherosclerosis include diabetes mellitus, hypercholesterolemia, cigarette smoking, and hypertension.[45,47,48]

Intracranial stenosis is usually detected in patients who present with an acute stroke. Most published data on the natural history of intracranial atherosclerosis are derived from patients examined either by conventional angiography or by transcranial Doppler ultrasonography. The natural history remains elusive: Intracranial stenoses may undergo progression, regression, or remain stable during the follow-up period.[42,49–51] Some reports suggest that intracranial stenoses diagnosed in the setting of acute cerebrovascular events or during angiographic (invasive or noninvasive) evaluation before planned carotid artery revascularization will regress with medical treatment, which raises important questions about the pathophysiology of the process. Current imaging techniques cannot determine the future course of a given lesion, and the precise nature of the underlying lesion, ie, local thrombosis or atherosclerosis, is difficult to distinguish.

Prognosis after stroke associated with intracranial stenoses may be dependent on location and extent of intracranial atherosclerosis. Most of our knowledge about the natural history of intracranial atherosclerosis is based on a number of retrospective series, which are summarized in Table 3.[48,52–60]

Antithrombotic Therapy for Intracranial Stenoses

The first Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Study was a retrospective analysis of outcomes in

Table 3. Annual Death and Stroke Rates According to the Distribution of Stenosis in Intracranial Atherosclerosis

Disease Distribution	Death Rate per Annum, %	Any Stroke per Annum, %	Isotopic Stroke per Annum, %	References
Carotid	9.5–17.2	3.9–11.7	3.1–8.1	48, 52–55
MCA	3.3–7.7	2.8–4.2	4.7	56–58
Vertebrobasilar	6.1–9.7	2.4–13.1	0–8.7	59, 60

MCA indicates middle cerebral artery.

patients with symptomatic severe intracranial arterial disease who had been treated with either aspirin or warfarin.[61] During a median follow-up time of 14.7 months, the major vascular event rate (defined as stroke, myocardial infarction, or sudden death) was 8.4 per 100 patient-years in the warfarin-treated group, whereas during a median follow-up of 19.3 months, the rate of major vascular events was 18.1 per 100 patient-years in the aspirin-treated group. The first WASID study was retrospective, and treatment was not standardized. Therefore, it did not determine the optimal antithrombotic therapy for symptomatic intracranial arterial stenosis.

Thijs et al[62] described a series of 52 patients with transient ischemic attacks or stroke due to intracranial atherosclerotic stenosis. Twenty-nine patients (56%) had additional transient ischemic attacks or stroke while receiving antithrombotic therapy, such as warfarin, heparin, or antiplatelet agents. Twenty-five patients were eligible for the follow-up after failing antithrombotic therapy. Fifteen (60%) of these patients had a TIA or stroke or died during follow-up. The median time to TIA, stroke, or death was 36 days (95% CI 13 to 59). The 15 outcome events were TIA (n=7), nonfatal stroke (n=6), fatal stroke (n=1), and death due to retroperitoneal hemorrhage while receiving heparin (n=1).[62]

The second WASID trial was a prospective, multicenter, randomized, double-blind National Institutes of Health–funded study, performed from 1998 to 2003; it was based on the earlier, retrospective first WASID trial data.[63] The second WASID trial compared the efficacy and safety of aspirin with warfarin in patients with intracranial stenosis. Patients with transient ischemic attack or minor stroke caused by an angiographically verified stenosis greater than 50% of a major intracranial artery were randomized to either warfarin (international normalized ratio 2 to 3) or aspirin (1300 mg per day). The primary study end point was ischemic stroke, brain hemorrhage, or death of vascular causes other than stroke. There was no difference in the occurrence rate of the primary study end point between the 2 treatment arms (aspirin 22.1%, warfarin 21.8%, hazard ratio 1.04, 95% CI 0.73 to 1.48, $P=0.83$). Adverse outcome events were more frequent in the warfarin group than among aspirin-allocated patients (death 9.7% versus 4.3%; major hemorrhage 8.3% versus 3.2%; myocardial infarct and sudden death 7.3% versus 2.9%). The trial was terminated prematurely after 569 patients had undergone randomization because of concerns about the safety of the patients who had been assigned to receive warfarin.[63]

Additional analysis of WASID provided important information about the risk for stroke after the qualifying ischemic event.[64] In a multivariable model that was adjusted for age, gender, and race, the risk of stroke in the territory of the stenotic artery was highest with severe stenosis ≥70% (hazard ratio 2.00, 95% CI 1.25 to 3.19, $P=0.0026$) and in patients enrolled early (≤17 days) after the qualifying event (hazard ratio 1.72, 95% CI 1.07 to 2.78, $P=0.026$).[64]

The WASID authors concluded that "these data indicate that intracranial stenosis is a high-risk disease for which alternative therapies are needed. Other options include aggressive management of risk factors, alternative antiplatelet regimens, and intracranial angioplasty or stenting. As yet, none of these treatments have been evaluated in a controlled clinical trial in patients with intracranial stenosis" (pp 1313–1314).[63]

Endovascular Treatment of Intracranial Stenoses

Improvements in microcatheter technology have allowed for innovative endovascular neurovascular procedures. The use of intracranial angioplasty and stenting for treatment of patients with high-grade, symptomatic, or severe asymptomatic intracranial atherosclerotic disease at high risk for a stroke has been the subject of individual reports, and its efficacy has been evaluated in a few prospective, multicenter trials.[65–67] Notably, the successful use of balloon angioplasty for the treatment of intracranial atherosclerosis has been reported by an increasing number of medical centers, predominantly academic and high-volume medical centers with significant neurovascular expertise.[68] Results are encouraging, yet the procedure is technically demanding at many levels and carries substantial risk.

A recent meta-analysis of all retrospective and prospective case series published until March 2006 found periinterventional rates of 7.9% (95% CI 5.5% to 10.4%) for stroke, 3.4% (95% CI 2.0% to 4.8%) for death, and 9.5% (95% CI 7.0% to 12.0%) for stroke or death.[69] Since publication of this report, several additional series of symptomatic patients with intracranial stenosis have been published with similar rates for periinterventional stroke and death.[68,70–79]

The first prospective study, the SSYLVIA trial (Stenting of SYmptomatic atherosclerotic Lesions in the Vertebral or Intracranial Arteries), was a multicenter, nonrandomized, prospective feasibility study that evaluated the Neurolink intracranial stent system (Guidant, Santa Clara, Calif) for the treatment of extracranial vertebral or intracranial cerebral artery stenosis.[65] Sixty-one patients 18 to 80 years of age with symptoms attributed to a single arterial stenosis with >50% stenosis were included. Forty-three (70.5%) had an intracranial stenosis, and 18 (29.5%) had an extracranial vertebral artery stenosis. The 30-day stroke and mortality rates were 6.6% and 0%, respectively. Successful stent placement was achieved in 58 (95%) of 61 cases. At 6 months, 32.4% of intracranial vessels and 42.9% of extracranial vertebral arteries that were treated by stenting had restenosis. Seven (39%) of these recurrent stenoses were symptomatic. Four (7.3%) of 55 patients had strokes between 30 days and 1 year after intervention. Sixty-one percent of the restenosis patients remained asymptomatic. On the basis of this study, the US FDA granted the company a humanitarian device exemption

to use balloon angioplasty and stent placement to treat high-risk patients with significant intracranial and extracranial atherosclerotic disease for which medical therapy had failed.[80] However, the risk of treatment raises questions about whether intracranial stenting alters the natural history of the disease and improves the long-term outcome of these patients. This study was not powered to show these end points, and there was no control group.

In 2005, Henkes et al[66] reported the initial Wingspan (Boston Scientific) trial data, followed by additional trial data presented to the US FDA.[67] The Wingspan technique represented a new concept in cerebral artery revascularization by use of balloon angioplasty followed by placement of a self-expanding nitinol microstent across the atherosclerotic lesion in the brain. Revascularization with the Wingspan stent was performed in 45 patients with symptomatic intracranial atherosclerosis >50%, who were enrolled from 12 European sites. Of these cases, 95% had prior strokes, and 29% had transient ischemic attacks. Technical success for angioplasty of the stenosis and stent deployment was achieved in 98% (44/45) of cases. The composite 30-day rate of death or ipsilateral stroke was 4.5% (2/44), the 6-month death or ipsilateral stroke rate was 7.1% (3/42), and the 6-month all-cause stroke rate was 9.5% (4/42).[67] On the basis of these data, the US FDA granted humanitarian device exemption approval for the Wingspan stent system in 2005 to treat symptomatic patients with an intracranial stenosis >50% that was refractory to medical therapy. Approval for this stent system was also obtained in Europe.

In 2007, a consortium of 4 cerebrovascular treatment centers published a series of 78 patients with 82 symptomatic intracranial stenoses with ≥50% luminal narrowing, all treated with the Wingspan intracranial stent system. Stent implantation was achieved ("technical success") in 98.8%. The composite ipsilateral stroke and death rate was 4.5% at 30 days.[81] At short-term follow-up, 10.2% of patients developed symptomatic restenosis in the territory of the initially treated vessel.[78] The authors concluded that revascularization with the Wingspan system is a viable treatment option in this patient population; however, high rates of early restenosis, up to 30% in the aggregate during short-interval follow-up, have been described and raise questions about the durability of this particular technology and approach to treatment.[76,82] A second registry funded by the National Institutes of Health studied 129 patients at 16 medical centers and found that there was a 14% rate of stroke, hemorrhage, or death at 30 days or ipsilateral stroke at 6-month follow-up.[83] The value of stent-assisted angioplasty in the treatment of intracranial atherosclerosis remains to be established. A phase III clinical trial called SAMMPRIS (Stenting and Aggressive Medical Management for Preventing Stroke in Intracranial Stenosis), funded by the National Institute of Neurological Disorders and Stroke (NINDS), will compare intracranial stenting with best medical therapy in carefully selected patients with symptomatic intracranial arterial stenosis.[84] The trial began recruiting patients in November 2008.

Recommendations

1. Patients with intracranial stenoses should receive advice about lifestyle modification and treatment of atherosclerotic risk factors with statins, angiotensin-converting enzyme inhibitors, and antithrombotics as recommended by the AHA/American Stroke Association guidelines for secondary stroke prevention[85] (*Class I, Level of Evidence A*).
2. Endovascular revascularization by intravascular balloon angioplasty and/or stenting may be considered for patients with symptomatic severe intracranial stenoses (>70% luminal narrowing) despite optimal medical therapy (*Class IIb, Level of Evidence C*).

Acute Ischemic Stroke

Intra-Arterial Thrombolysis

Stroke is the third-leading cause of death in the United States, Europe, Canada, China, Korea, and Japan. There are more than 750 000 new strokes each year, which cause more than 200 000 deaths annually in the United States at a cost of more than $57 billion.[40] The vast majority of strokes are ischemic, and stroke is the major cause of adult disability. Recombinant tissue plasminogen activator (rtPA), a thrombolytic agent, is currently the only drug to receive FDA approval for treatment of ischemic stroke (via intravenous administration). Among the large number of stroke trials performed during the last decade, the only 2 successful intravenous stroke thrombolysis trials were part 1 and part 2 of the NINDS rtPA trials. These resulted in FDA approval of intravenous thrombolysis with rtPA for the treatment of ischemic stroke in selected patients within 3 hours after stroke onset.[86] This is now considered worldwide as "standard of care."

Recent surveys indicate that intra-arterial thrombolysis is used less frequently than intravenous thrombolysis. According to 1999 to 2001 National Hospital Discharge Survey data, there were 1 796 513 admissions for ischemic stroke between 1999 and 2001.[87] Of these admissions, 1314 (0.07%) were treated by intra-arterial thrombolysis, and 11 283 (0.6%) received intravenous thrombolytic therapy. Another estimate of thrombolytic therapy treatment for acute ischemic stroke is derived from the Greater Buffalo and Erie County stroke study.[88] Intravenous and intra-arterial thrombolysis was used in 1.4% and 0.3% of 1590 patients admitted to 11 hospitals, respectively.

Intra-arterial thrombolysis is typically considered when patients miss the therapeutic 3-hour window for intravenous thrombolysis. Some stroke centers use intra-arterial thrombolysis within 3 hours after stroke onset either as primary intervention or as rescue intervention after systemic 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.[89] Mechanical revascularization may be beneficial in occluded cerebral arteries with a large clot burden.

Recanalization depends on the cerebral artery and the location of the occlusion within the artery. For example, as assessed by validated transcranial Doppler criteria (Throm-

bolysis in Brain Ischemia [TIBI] flow grades), treatment with intravenous rtPA demonstrated complete recanalization in 50 (44%) of 113 patients with distal middle cerebral artery occlusion, 49 (30%) of 163 patients with proximal middle cerebral artery occlusion, 1 (6%) of 17 patients with terminal internal carotid artery occlusion, 6 (27%) of 22 patients with tandem cervical internal carotid artery and middle cerebral artery occlusion, and 3 (30%) of 10 patients with basilar artery occlusion.[90] Complete recanalization translates into improved overall clinical outcome: Patients with minimal or no recanalization have a worse outcome than patients with complete recanalization.[90]

The value of intra-arterial thrombolysis to improve patient outcomes remains controversial given the lack of adequately designed and powered randomized, prospective trials, and current evidence is mostly derived from case series (see Mandava and Kent for review[91]). Even for basilar artery occlusion, with its high risk of severe associated morbidity and mortality, intra-arterial thrombolysis remains controversial.[92–95] Intra-arterial thrombolysis has been tested only in a few controlled trials. The safety and efficacy of intra-arterial administration of recombinant prourokinase for treatment of middle cerebral artery occlusion of less than 6 hours' duration were demonstrated in the Prolyse in Acute Cerebral Thromboembolism Trial (PROACT-I).[96] Subsequently, the clinical efficacy of intra-arterial thrombolysis with recombinant prourokinase for middle cerebral artery occlusion was confirmed in PROACT-II, which was completed in 1998. In PROACT-II, patients with National Institutes of Health Stroke Scale (NIHSS) scores between 4 and 30 (median NIHSS 17) were screened with angiography.[89] As in PROACT-I, major exclusion criteria included intracranial hemorrhage, infarction of greater than one third of the middle cerebral artery distribution on computed tomographic brain scan, and stroke syndrome greater than 6 hours in duration. A total of 180 patients were randomized in a 2:1 manner to receive 9 mg of prourokinase, which was administered directly onto an angiographically proven middle cerebral artery occlusion, plus low-dose heparin (2000-IU bolus with 500 IU per hour for 4 hours) or low-dose heparin alone. The primary outcome measure was the percentage of patients who achieved a modified Rankin score less than 2 at 90 days after ictus. Secondary measures included the percentage of patients with NIHSS $\leq$1 at 90 days, angiographic recanalization, symptomatic intracranial hemorrhage, and death. PROACT-II demonstrated a 15% absolute benefit in the number of patients who achieved modified a Rankin score less than 2 at 90 days. Recanalization at 2 hours was achieved in 66% of the prourokinase group versus 18% of the heparin-only (control) group; symptomatic hemorrhage by 24 hours occurred in 10% of the prourokinase group versus 2% of the control group.[89] Like the NINDS trial, administration of the thrombolytic drug resulted in a higher rate of early symptomatic brain hemorrhage; however, patients benefited from treatment, and there was no excess mortality (24% for prourokinase plus heparin versus 27% for heparin only). The results were encouraging but did not result in FDA approval.

A small, randomized, multicenter trial compared intravenous urokinase with intra-arterial urokinase administered within the first 6 hours of acute ischemic stroke.[97] Patients were randomly assigned to receive either intravenous (n=14) or intra-arterial (n=13) urokinase (each 900 000 U). The study was terminated prematurely because 7 patients (26%) died, 4 in the intravenous group and 3 in the intra-arterial group. Recently, a case-control study was reported from Japan's Multicenter Stroke Investigator's Collaboration (J-MUSIC).[98] Clinical outcomes for 91 patients who presented within 4.5 hours after stroke onset and received intra-arterial 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 of 0 to 2) was observed more frequently in the urokinase group (51%) than in the control group (34%). A third study[99] randomized 16 patients with angiographic evidence of posterior circulation vascular occlusion who presented within 24 hours of symptom onset to either intra-arterial urokinase or conservative management. There was some imbalance between groups, with greater severity of deficit at baseline observed in the urokinase treatment arm. Good outcomes were observed in 4 of 8 patients who received intra-arterial urokinase and in 1 of 8 patients in the control group.

Recanalization rates for major cerebrovascular occlusions with the intra-arterial therapy approach were 70% compared with 34% with intravenous thrombolysis.[89] This difference was most apparent in patients with internal carotid, carotid terminus, or proximal middle cerebral artery occlusions. Despite the uncontrolled observation that recanalization rates may be higher with intra-arterial thrombolysis than with intravenous thrombolysis,[100] clinical benefit may be counterbalanced by delays to initiation of treatment with the intra-arterial approach. The AHA/American Stroke Association 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 hours' duration due to occlusions of the middle cerebral artery who are not otherwise candidates for intravenous rtPA.[101]

Recently, emphasis has been placed on deriving information from the initial angiogram to determine the site of occlusion and identify the collateral supply to the affected region. New data suggest that this information may be incorporated into a scheme to stratify patients into expected rates of recanalization and short-term outcome after intra-arterial thrombolysis.[100,102] For instance, proximal occlusions of the intracranial internal carotid artery and the middle cerebral artery stem demonstrate low recanalization rates, 8% and 26%, respectively, after intravenous administration of thrombolytic agents.[103,104]

Several recent trials have explored the adjunctive role of endovascular methods with intravenous thrombolytic therapy to treat acute stroke. The Emergency Management of Stroke (EMS) trial was a phase 1 pilot trial that randomized patients to a partial dose of an intravenous thrombolytic drug (alte-

plase 0.6 mg/kg) versus intravenous placebo. Both groups then underwent arteriography and received up to 20 mg of intra-arterial alteplase for acute middle cerebral artery occlusion.[105] Arteriography did not demonstrate vessel occlusion in one third of patients in the angiogram performed after low-dose intravenous thrombolysis. Good outcomes were achieved in 66% of 15 patients with M1 or M2 middle cerebral artery occlusions at a mean time to treatment of 4.2 hours. Although bridging intravenous with intra-arterial thrombolytic therapy achieved a higher rate of recanalization, there was no significant difference in functional outcomes between the 2 groups.

Interventional Management of Stroke (IMS) is a series of studies that explored the combination of intravenous with intra-arterial thrombolytic therapies when early recanalization did not occur after intravenous therapy alone. In IMS-1, a bridging, or partial dose, of intravenous rtPA (0.6 mg/kg) within 3 hours of stroke onset was combined with intra-arterial rtPA (≤22 mg). Outcomes were compared with patients in the placebo and intravenous rtPA–treated subjects from the NINDS rt-PA Stroke Trial.[106] IMS-1 showed improved clinical outcomes compared with the NINDS rt-PA Stroke Trial placebo group despite a statistically significant increase (6.3%) in symptomatic hemorrhage; however, IMS-1 patients showed no better functional outcomes than patients in the NINDS rt-PA Stroke Trial who received intravenous thrombolytic therapy.[106] IMS-2 was designed to test combined intravenous and intra-arterial rtPA with a novel intra-arterial ultrasound infusion system designed by EKOS Corp (Bothell, Wash). The EKOS microinfusion catheter (Primo catheter) uses acoustic streaming to increase fluid permeation, thus driving the thrombolytic agent into the thrombus. In IMS-2, 55 patients received intravenous thrombolysis followed by intra-arterial intervention (36 patients by sonography microcatheter and 19 by standard microcatheter).[107] Among the 29 patients treated with the Primo catheter and sonography activation, complete recanalization was achieved within 60 minutes in 12 (41%) and within 120 minutes in 20 (68.9%). The authors chose to compare these results to findings from control patients in IMS-1. Complete recanalization was achieved in 7 (30.4%) of the 23 control patients from the IMS-1 trial. Overall, the pooled analysis based on IMS-1 and IMS-2 showed that complete recanalization was achieved within 120 minutes in 68.9% of patients with the EKOS Primo catheter with sonography activation compared with 53.3% of patients by use of either the EKOS Primo catheter without sonography activation or IMS-1 standard microcatheter intervention. Successful revascularization correlated with good outcome. IMS-3 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.[108] If additional intra-arterial stroke devices achieve FDA approval, these may be added to the protocol.

Other studies are also in progress to evaluate the efficacy of drugs and devices for acute ischemic stroke treatment. The use of perfusion-weighted magnetic resonance imaging to assess response to intravenous thrombolysis and as a basis for intra-arterial treatment can improve clinical outcomes beyond those in the IMS trials.

Recommendations

Current indications for intra-arterial thrombolysis by appropriately qualified and certified physicians include the following:

1. Intra-arterial thrombolysis is indicated for treatment of selected patients with major stroke of <6 hours' duration due to an occlusion of the middle cerebral artery (*Class I, Level of Evidence B*). (This recommendation has not changed since the publication of previous guidelines.[109])
2. Intra-arterial thrombolysis is reasonable for patients who have contraindications to the use of intravenous thrombolysis, such as recent surgery (*Class IIa, Level of Evidence C*). (This recommendation was not included in the previous guidelines.)
3. The availability of intra-arterial thrombolysis should generally not preclude the intravenous administration of rtPA in otherwise eligible patients (*Class I, Level of Evidence A*).
4. 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 (*Class I, Level of Evidence C*).

Mechanical Clot Extraction

A number of medical devices have been used over the past decade to extract thrombi from occluded intracranial arteries in patients with an acute ischemic stroke.[110,111] In the Mechanical Embolus Removal in Cerebral Embolism (MERCI) trial, vessels were opened within 8 hours from symptom presentation with a device that removed the thrombus from an intracranial artery.[112] Rapid opening of the artery was achieved, but overall efficacy and safety achieved with the MERCI retrieval system were similar to those that occurred with intra-arterial prourokinase in the PROACT-II trial.[89] For instance, the rate of recanalization of the middle cerebral artery in MERCI was 45%, and it was 66% in PROACT-II. In the MERCI trial, 17 patients received thrombolytic medications when the device was unable to achieve adequate recanalization, but the outcomes of these specific patients were not reported separately. The FDA has approved the MERCI device for reopening intracranial arteries in acute ischemic stroke. Its clinical efficacy, however, has not been fully established in a controlled outcomes trial.

Multi-MERCI was a multicenter, prospective, single-arm trial of thrombectomy that included 177 patients with moderate-to-severe large-vessel ischemic strokes.[113] Eligible patients were those within 8 hours of stroke onset who had either failed to respond to intravenous rtPA or were ineligible for intravenous rtPA but were still eligible for intra-arterial treatment. The thrombectomy device was deployed successfully in 164 patients. Recanalization was achieved in 55% of patients with the thrombectomy device alone; the percentage of recanalized vessels increased to 68% with combined mechanical and intra-arterial thrombolytic therapy. Symp-

tomatic intracranial hemorrhage occurred in 9.8% of patients, and significant procedural complications occurred in 5.5% of patients. Good neurological outcomes (modified Rankin scale score ≤2) were observed in 36% of patients at 90 days; however, there was a 34% mortality rate at 90 days. The high mortality may be due to the stroke severity of the cohort (mean NIHSS 19 points, interquartile range 15 to 23). A recent trial of mechanical clot extraction with the Penumbra System (Penumbra, Inc, San Leandro, Calif), a device designed to revascularize large-vessel occlusions in the intracranial circulation, was completed recently, and its publication in a peer-reviewed journal is pending.

Angioplasty and Stenting

Limited data are available about the use of angioplasty and stenting in the emergency treatment of intracranial or extracranial lesions in patients with an acute ischemic stroke.[114–117] Jovin et al[118] achieved recanalization in 23 of 25 patients by emergency stenting of a total occlusion of the extracranial internal carotid artery in the setting of an acute (n=15) or subacute (n=8) ischemic stroke. Brekenfeld et al[119] treated 350 patients with intra-arterial urokinase and observed increased recanalization rates with adjunctive angioplasty and stenting. Angioplasty with or without stenting also has been combined with emergency administration of thrombolytic agents in patients with occlusions in the vertebrobasilar circulation. A retrospective review of patients treated with stenting and angioplasty for intracranial occlusions found a 90% recanalization rate.[120] Angioplasty plus stenting also has been used to treat patients with acute stroke secondary to carotid artery dissection.[121]

Recommendations

1. Although the Concentric Merci device can be useful for extraction of intra-arterial thrombi in appropriately selected patients, the utility of the device in improving outcomes after stroke remains unclear (*Class IIb, Level of Evidence B*).
2. The usefulness of other endovascular devices is not yet established, but they may be beneficial. (*Class IIb, Level of Evidence C*).

Arteriovenous Malformations and Dural Fistulas

Cerebral Arteriovenous Malformations

Intracranial arteriovenous malformations (AVMs) are an uncommon but important cause of serious neurological disability or death. Advancements are being made in our understanding of the cause, prevalence, incidence, and natural history of these lesions, as well as the effect of treatment. The exact prevalence of cerebral AVMs in the United States is not known. The AVM detection rate in the general population based on prospective data from the New York Islands AVM Study is approximately 1.34 per 100 000 person-years.[122] Elsewhere, the detection rate is 1.11 per 100 000 person-years.[123,124] The prevalence of brain AVMs is so low, however, that any estimate of prevalence rate will be limited by population size.[125] Approximately half of all cases (0.55 per 100 000 patient-years) present with hemorrhage,[126] but the most common mode of presentation is probably seizures.[124,127] The risk of hemorrhage has been estimated to range from 2% to 4%, but recently, these risk point estimates have been challenged.[128] Lifetime risk can be estimated roughly by subtracting the patient's age from 105.[129] With neuroimaging techniques, many AVMs are now discovered before they cause brain hemorrhage. In the only prospective determination of hemorrhage risk, the annual risk was 2% for AVMs that had not already hemorrhaged. The risk was dramatically higher for patients with prior hemorrhage: 32.9% during the first year and 11.3% thereafter.[130]

The standard of treatment and cure remains surgical excision. Other treatments include endovascular surgery with embolization and focused radiosurgery. Surgical morbidity can be improved by preoperative endovascular embolization in selected cases. Preoperative embolization was performed with a low risk of permanent, disabling neurological deficit (2% to 3%).[131,132] An outcomes trial comparing natural history with modern multimodality therapy over 5 years has recently received funding from the National Institutes of Health.[128]

Dural Arteriovenous Fistulas

Dural arteriovenous fistulas, or dural AVMs, are acquired artery-to-vein shunts within the dura mater, often without a distinctive vascular nidus. They constitute 10% to 15% of all intracranial AVMs.[133] Symptoms depend on the location of the fistula and range from pulse-synchronous tinnitus and exophthalmos to cranial nerve deficits, dementia, venous infarct, intracranial hemorrhage, and even death. Unlike AVMs of the brain parenchyma, dural fistulas are often amenable to curative endovascular treatment with contemporary transvenous or transarterial embolization techniques. Similarly, certain pediatric fistulas, including the vein of Galen malformation, may be amenable to curative occlusion by endovascular techniques. Compared with some surgical series in which 90% of children with vein of Galen malformations died at surgery and the remainder remained severely disabled, up to 80% of cases can now be palliated or cured by use of endovascular techniques, with good to excellent functional outcomes.[134,135]

Recommendations

1. Endovascular techniques for treatment of AVMs and dural arteriovenous fistulas may be considered in certain circumstances (*Class IIb, Level of Evidence C*).
2. Endovascular treatment for dural fistulas may be curative, although it is usually adjunctive therapy for pial brain AVMs (*Class IIb, Level of Evidence C*).

Acknowledgments

We wish to acknowledge Kathryn A. Taubert, PhD, for helping to build multidisciplinary participation and support for this manuscript and for her assistance navigating the review process.

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board	Other
Philip M. Meyers	Columbia University, College of Physicians & Surgeons; New York Presbyterian Hospitals	None	None	None	None	None	None
H. Christian Schumacher	Albert Einstein College of Medicine, The Saul R. Korey Department of Neurology	None	None	Concentric Medical, Inc*	None	None	None
Randall T. Higashida	Radiology and Neurosurgery, University of California, San Francisco Medical Center	None	None	None	None	Cordis Neurovascular*; Concentric Medical*; Nuvelo, Inc*	None
Stanley L. Barnwell	Oregon Health & Science University	None	None	None	None	Boston Scientific*; Cordis*; ev3*; NeuroVasx*; WL Gore*	None
Mark A. Creager	Brigham & Women's Hospital, Boston, Mass	None	None	None	None	None	None
Rishi Gupta	Cleveland Clinic	None	None	None	None	Concentric Medical*	None
Cameron G. McDougall	Barrow Neurosurgical Associates	None	None	None	None	Boston Scientific*; Cordis*; ev3*	None
Dilip K. Pandey	University of Illinois at Chicago	None	None	None	None	None	None
David Sacks	Reading Hospital	None	None	None	Angiotech Pharmaceuticals (stockholder)†	Arrow International (consultant)*; PneumRx (consultant)*	None
Lawrence R. Wechsler	University of Pittsburgh School of Medicine	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Colin Derdeyn	Washington University	NIH†; Genentech, Inc†	None	None	None	nFocus*	W.L. Gore and Associates†	None
Huy Do	Stanford University	None	None	None	None	None	None	None
Mary Lee Jensen	University of Virginia	None	None	None	None	None	None	None
Manesh Patel	Duke University	None	None	None	None	None	None	None
Christopher White	Ochsner Medical Institutions	None	None	None	None	None	Baxter Scientific Advisory Board*	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

References

1. Accreditation Council for Graduate Medical Education. ACGME program requirements for fellowship education in endovascular surgical neuroradiology. Available at: http://www.acgme.org/acwebsite/downloads/rrc_progreq/422endovascularneuroradiology07012007.pdf. Accessed May 2008.
2. Higashida RT, Hopkins LN, Berenstein A, Halbach VV, Kerber C. Program requirements for residency/fellowship education in neuroendovascular surgery/interventional neuroradiology: a special report on graduate medical education. *AJNR Am J Neuroradiol*. 2000;21:1153–1159.
3. Creager MA, Goldstone J, Hirshfeld JW Jr, Kazmers A, Kent KC, Lorell BH, Olin JW, Rainer Pauly R, Rosenfield K, Roubin GS, Sicard GA,

White CJ, Winters WL Jr, Merli G, Rodgers GP, Tracy CM, Weitz HH. ACC/ACP/SCAI/SVMB/SVS clinical competence statement on vascular medicine and catheter-based peripheral vascular interventions: a report of the American College of Cardiology/American Heart Association/American College of Physicians Task Force on Clinical Competence (ACC/ACP/SCAI/SVMB/SVS Writing Committee to develop a clinical competence statement on peripheral vascular disease). *J Am Coll Cardiol*. 2004;44:941–957.

4. Bederson JB, Awad IA, Wiebers DO, Piepgras D, Haley EC Jr, Brott T, Hademenos G, Chyatte D, Rosenwasser R, Caroselli C. Recommendations for the management of patients with unruptured intracranial aneurysms: a statement for healthcare professionals from the Stroke Council of the American Heart Association. *Stroke*. 2000;31:2742–2750.
5. Kiyohara Y, Ueda K, Hasuo Y, Wada J, Kawano H, Kato I, Sinkawa A, Ohmura T, Iwamoto H, Omae T. Incidence and prognosis of subarachnoid hemorrhage in a Japanese rural community. *Stroke*. 1989;20:1150–1155.
6. Sarti C, Tuomilehto J, Salomaa V, Sivenius J, Kaarsalo E, Narva EV, Salmi K, Torppa J. Epidemiology of subarachnoid hemorrhage in Finland from 1983 to 1985. *Stroke*. 1991;22:848–853.
7. van Gijn J, Rinkel GJ. Subarachnoid haemorrhage: diagnosis, causes and management. *Brain*. 2001;124(pt 2):249–278.
8. Inagawa T, Hirano A. Autopsy study of unruptured incidental intracranial aneurysms. *Surg Neurol*. 1990;34:361–365.
9. McCormick WF, Nofzinger JD. Saccular intracranial aneurysms: an autopsy study. *J Neurosurg*. 1965;22:155–159.
10. Schievink WI. Intracranial aneurysms [published correction appears in *N Engl J Med*. 1997;336:1267]. *N Engl J Med*. 1997;336:28–40.
11. Mayberg MR, Batjer HH, Dacey R, Diringer M, Haley EC, Heros RC, Sternau LL, Torner J, Adams HP Jr, Feinberg W. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke*. 1994;25:2315–2328.
12. McKissock W, Richardson A, Walsh L. Anterior communicating aneurysms: a trial of conservative and surgical treatment. *Lancet*. 1965;1:874–876.
13. Hop JW, Rinkel GJ, Algra A, van Gijn J. Case-fatality rates and functional outcome after subarachnoid hemorrhage: a systematic review. *Stroke*. 1997;28:660–664.
14. Guglielmi G, Viñuela F, Dion J, Duckwiler G. Electrothrombosis of saccular aneurysms via endovascular approach: part 2: preliminary clinical experience. *J Neurosurg*. 1991;75:8–14.
15. Guglielmi G, Viñuela F, Sepetka I, Macellari V. Electrothrombosis of saccular aneurysms via endovascular approach: part 1: electrochemical basis, technique, and experimental results. *J Neurosurg*. 1991;75:1–7.
16. Food and Drug Administration Web Site. Onyx liquid embolic system (Onyx HD-500): h060003. Approved April 11, 2007. Available at: http://www.fda.gov/cdrh/ode/h060003sum.html. Accessed August 4, 2008.
17. Henkes H, Bose A, Felber S, Miloslavski E, Berg-Dammer E, Kuhne D. Endovascular coil occlusion of intracranial aneurysms assisted by a novel self-expandable nitinol microstent (Neuroform). *Interv Neuroradiol*. 2002;8:107–119.
18. Food and Drug Administration Web Site. Neuroform microdelivery stent system: h020002. Issued September 11, 2002. Available at: http://www.fda.gov/cdrh/ode/H020002sum.html. Accessed August 4, 2008.
19. Higashida RT, Halbach VV, Dowd CF, Juravsky L, Meagher S. Initial clinical experience with a new self-expanding nitinol stent for the treatment of intracranial cerebral aneurysms: the Cordis Enterprise stent. *AJNR Am J Neuroradiol*. 2005;26:1751–1756.
20. Fiorella D, Woo HH, Albuquerque FC, Nelson PK. Definitive reconstruction of circumferential, fusiform intracranial aneurysms with the pipeline embolization device. *Neurosurgery*. 2008;62:1115–1120.
21. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, Holman R; International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet*. 2002;360:1267–1274.
22. Molyneux AJ, Kerr RS, Yu LM, Clarke M, Sneade M, Yarnold JA, Sandercock P; International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet*. 2005;366:809–817.
23. Campi A, Ramzi N, Molyneux AJ, Summers PE, Kerr RS, Sneade M, Yarnold JA, Rischmiller J, Byrne JV. Retreatment of ruptured cerebral aneurysms in patients randomized by coiling or clipping in the International Subarachnoid Aneurysm Trial (ISAT). *Stroke*. 2007;38:1538–1544.
24. CARAT Investigators. Rates of delayed rebleeding from intracranial aneurysms are low after surgical and endovascular treatment. *Stroke*. 2006;37:1437–1442.
25. Wiebers DO, Whisnant JP, Huston J III, Meissner I, Brown RD Jr, Piepgras DG, Forbes GS, Thielen K, Nichols D, O'Fallon WM, Peacock J, Jaeger L, Kassell NF, Kongable-Beckman GL, Torner JC; International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362:103–110.
26. Higashida RT, Lahue BJ, Torbey MT, Hopkins LN, Leip E, Hanley DF. Treatment of unruptured intracranial aneurysms: a nationwide assessment of effectiveness. *AJNR Am J Neuroradiol*. 2007;28:146–151.
27. Johnston SC, Dudley RA, Gress DR, Ono L. Surgical and endovascular treatment of unruptured cerebral aneurysms at university hospitals. *Neurology*. 1999;52:1799–1805.
28. Raymond J. Trial on Endovascular Aneurysm Management (TEAM). Available at: http://www.teamstudy.org/index.html. Accessed May 28, 2008.
29. Meisel HJ, Mansmann U, Alvarez H, Rodesch G, Brock M, Lasjaunias P. Cerebral arteriovenous malformations and associated aneurysms: analysis of 305 cases from a series of 662 patients. *Neurosurgery*. 2000;46:793–800.
30. Perata HJ, Tomsick TA, Tew JM Jr. Feeding artery pedicle aneurysms: association with parenchymal hemorrhage and arteriovenous malformation in the brain. *J Neurosurg*. 1994;80:631–634.
31. Cloft HJ, Kallmes DF, Kallmes MH, Goldstein JH, Jensen ME, Dion JE. Prevalence of cerebral aneurysms in patients with fibromuscular dysplasia: a reassessment. *J Neurosurg*. 1998;88:436–440.
32. Anxionnat R, de Melo Neto JF, Bracard S, Lacour JC, Pinelli C, Civit T, Picard L. Treatment of hemorrhagic intracranial dissections. *Neurosurgery*. 2003;53:289–300.
33. Mizutani T, Kojima H, Asamoto S, Miki Y. Pathological mechanism and three-dimensional structure of cerebral dissecting aneurysms. *J Neurosurg*. 2001;94:712–717.
34. Andersson R. Giant cell arteritis as a cause of death. *Clin Exp Rheumatol*. 2000;18(suppl 20):S27–S28.
35. Hurst RW, Grossman RI. Neuroradiology of central nervous system vasculitis. *Semin Neurol*. 1994;14:320–340.
36. Kovoor JM, Jayakumar PN, Srikanth SG, Sampath S. Intracranial infective aneurysms: angiographic evaluation with treatment. *Neurol India*. 2001;49:262–266.
37. Magge SN, Chen HI, Stiefel MF, Ernst L, Cahill AM, Hurst R, Storm PB. Multiple ruptured cerebral aneurysms in a child with Takayasu arteritis. *J Neurosurg Pediatr*. 2008;1:83–87.
38. Oh MS, Kim MH, Chu MK, Yu KH, Kim KH, Lee BC. Polyarteritis nodosa presenting with bilateral cavernous internal carotid artery aneurysms. *Neurology*. 2008;70:405.
39. Statler JD, Slaughter CR, Ronsivalle JA. Human immunodeficiency virus arteriopathy of the adult cerebral circulation. *Mil Med*. 2007;172:647–649.
40. American Heart Association. *Heart Disease and Stroke Statistics: 2006 Update.* Dallas, Tex: American Heart Association; 2006.
41. Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF. Lifetime cost of stroke in the United States. *Stroke*. 1996;27:1459–1466.
42. Wong KS, Huang YN, Gao S, Lam WW, Chan YL, Kay R. Intracranial stenosis in Chinese patients with acute stroke. *Neurology*. 1998;50:812–813.
43. Inzitari D, Hachinski VC, Taylor DW, Barnett HJ. Racial differences in the anterior circulation in cerebrovascular disease: how much can be explained by risk factors? *Arch Neurol*. 1990;47:1080–1084.
44. Resch JA, Okabe N, Loewenson RB, Kimoto K, Katsuki S, Baker AB. Pattern of vessel involvement in cerebral atherosclerosis: a comparative study between a Japanese and Minnesota population. *J Atheroscler Res*. 1969;9:239–250.

45. Wityk RJ, Lehman D, Klag M, Coresh J, Ahn H, Litt B. Race and sex differences in the distribution of cerebral atherosclerosis. *Stroke*. 1996; 27:1974–1980.
46. Sacco RL, Kargman DE, Gu Q, Zamanillo MC. Race-ethnicity and determinants of intracranial atherosclerotic cerebral infarction: the Northern Manhattan Stroke Study. *Stroke*. 1995;26:14–20.
47. Caplan LR, Gorelick PB, Hier DB. Race, sex and occlusive cerebrovascular disease: a review. *Stroke*. 1986;17:648–655.
48. Craig DR, Meguro K, Watridge C, Robertson JT, Barnett HJ, Fox AJ. Intracranial internal carotid artery stenosis. *Stroke*. 1982;13: 825–828.
49. Wong KS, Li H, Lam WW, Chan YL, Kay R. Progression of middle cerebral artery occlusive disease and its relationship with further vascular events after stroke. *Stroke*. 2002;33:532–536.
50. Segura T, Serena J, Castellanos M, Teruel J, Vilar C, Dávalos A. Embolism in acute middle cerebral artery stenosis. *Neurology*. 2001;56: 497–501.
51. Akins PT, Pilgram TK, Cross DT III, Moran CJ. Natural history of stenosis from intracranial atherosclerosis by serial angiography. *Stroke*. 1998;29:433–438.
52. Marzewski DJ, Furlan AJ, St Louis P, Little JR, Modic MT, Williams G. Intracranial internal carotid artery stenosis: longterm prognosis. *Stroke*. 1982;13:821–824.
53. Borozan PG, Schuler JJ, LaRosa MP, Ware MS, Flanigan DP. The natural history of isolated carotid siphon stenosis. *J Vasc Surg*. 1984;1: 744–749.
54. Wechsler LR, Kistler JP, Davis KR, Kaminski MJ. The prognosis of carotid siphon stenosis. *Stroke*. 1986;17:714–718.
55. Bogousslavsky J. Prognosis of carotid siphon stenosis. *Stroke*. 1987; 18:537.
56. Corston RN, Kendall BE, Marshall J. Prognosis in middle cerebral artery stenosis. *Stroke*. 1984;15:237–241.
57. Feldmeyer JJ, Merendaz C, Regli F. Symptomatic stenoses of the middle cerebral artery [in French]. *Rev Neurol (Paris)*. 1983;139:725–736.
58. Bogousslavsky J, Barnett HJ, Fox AJ, Hachinski VC, Taylor W. Atherosclerotic disease of the middle cerebral artery. *Stroke*. 1986;17: 1112–1120.
59. Moufarrij NA, Little JR, Furlan AJ, Leatherman JR, Williams GW. Basilar and distal vertebral artery stenosis: long-term follow-up. *Stroke*. 1986;17:938–942.
60. Pessin MS, Gorelick PB, Kwan ES, Caplan LR. Basilar artery stenosis: middle and distal segments. *Neurology*. 1987;37:1742–1746.
61. Chimowitz MI, Kokkinos J, Strong J, Brown MB, Levine SR, Silliman S, Pessin MS, Weichel E, Sila CA, Furlan AJ, Kargman DE, Sacco RL, Wityk RJ, Ford G, Fayad PB, for the Warfarin-Aspirin Symptomatic Intracranial Disease Study Group. The Warfarin-Aspirin Symptomatic Intracranial Disease Study. *Neurology*. 1995;45:1488–1493.
62. Thijs VN, Albers GW. Symptomatic intracranial atherosclerosis: outcome of patients who fail antithrombotic therapy. *Neurology*. 2000; 55:490–497.
63. Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, Levine SR, Chaturvedi S, Kasner SE, Benesch CG, Sila CA, Jovin TG, Romano JG; Warfarin-Aspirin Symptomatic Intracranial Disease Trial Investigators. Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. *N Engl J Med*. 2005;352: 1305–1316.
64. Kasner SE, Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, Levine SR, Chaturvedi S, Benesch CG, Sila CA, Jovin TG, Romano JG, Cloft HJ; Warfarin-Aspirin Symptomatic Intracranial Disease Trial Investigators. Predictors of ischemic stroke in the territory of a symptomatic intracranial arterial stenosis. *Circulation*. 2006;113:555–563.
65. SSYLVIA Study Investigators. Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA): study results. *Stroke*. 2004;35:1388–1392.
66. Henkes H, Miloslavski E, Lowens S, Reinartz J, Liebig T, Kühne D. Treatment of intracranial atherosclerotic stenoses with balloon dilatation and self-expanding stent deployment (WingSpan). *Neuroradiology*. 2005;47:222–228.
67. Food and Drug Administration (FDA), Center for Devices and Radiological Health. Wingspan Stent System With Gateway PTA Balloon Catheter: h050001. Approved August 3, 2005. Available at: http://www.Fda.Gov/cdrh/ode/h050001sum.html. Accessed May 28, 2008.
68. Marks MP, Wojak JC, Al-Ali F, Jayaraman M, Marcellus ML, Connors JJ, Do HM. Angioplasty for symptomatic intracranial stenosis: clinical outcome. *Stroke*. 2006;37:1016–1020.
69. Cruz-Flores S, Diamond AL. Angioplasty for intracranial artery stenosis. *Cochrane Database Syst Rev*. 2006;3:CD004133.
70. Abou-Chebl A, Krieger DW, Bajzer CT, Yadav JS. Intracranial angioplasty and stenting in the awake patient. *J Neuroimaging*. 2006;16: 216–223.
71. Terada T, Tsuura M, Matsumoto H, Masuo O, Tsumoto T, Yamaga H, Ohura Y, Itakura T. Hemorrhagic complications after endovascular therapy for atherosclerotic intracranial arterial stenoses. *Neurosurgery*. 2006;59:310–318.
72. Abruzzo TA, Tong FC, Waldrop AS, Workman MJ, Cloft HJ, Dion JE. Basilar artery stent angioplasty for symptomatic intracranial atheroocclusive disease: complications and late midterm clinical outcomes. *AJNR Am J Neuroradiol*. 2007;28:808–815.
73. Jiang WJ, Du B, Leung TW, Xu XT, Jin M, Dong KH. Symptomatic intracranial stenosis: cerebrovascular complications from elective stent placement. *Radiology*. 2007;243:188–197.
74. Jiang WJ, Xu XT, Du B, Dong KH, Jin M, Wang QH, Ma N. Long-term outcome of elective stenting for symptomatic intracranial vertebrobasilar stenosis. *Neurology*. 2007;68:856–858.
75. Steinfort B, Ng PP, Faulder K, Harrington T, Grinnell V, Sorby W, Morgan MK. Midterm outcomes of paclitaxel-eluting stents for the treatment of intracranial posterior circulation stenoses. *J Neurosurg*. 2007;106:222–225.
76. Turk AS, Ahmed A, Niemann DB, Aagaard-Kienitz B, Brooks N, Levine RL. Utilization of self-expanding stents in the treatment of intracranial atherosclerotic disease in the distal small cerebral vessels. *Neuroradiology*. 2007;49:659–663.
77. Wojak JC, Dunlap DC, Hargrave KR, DeAlvare LA, Culbertson HS, Connors JJ III. Intracranial angioplasty and stenting: long-term results from a single center. *AJNR Am J Neuroradiol*. 2006;27:1882–1892.
78. Gupta R, Al-Ali F, Thomas AJ, Horowitz MB, Barrow T, Vora NA, Uchino K, Hammer MD, Wechsler LR, Jovin TG. Safety, feasibility, and short-term follow-up of drug-eluting stent placement in the intracranial and extracranial circulation. *Stroke*. 2006;37:2562–2566.
79. Mazighi M, Yadav JS, Abou-Chebl A. Durability of endovascular therapy for symptomatic intracranial atherosclerosis. *Stroke*. 2008;39: 1766–1769.
80. Food and Drug Administration. Notice of humanitarian device exemption (HDE) for Neurolink(r) system. Available at: http://www.fda.gov/cdrh/pdf/h010004a.pdf. Accessed February 1, 2005.
81. Fiorella D, Levy EI, Turk AS, Albuquerque FC, Niemann DB, Aagaard-Kienitz B, Hanel RA, Woo H, Rasmussen PA, Hopkins LN, Masaryk TJ, McDougall CG. US multicenter experience with the Wingspan stent system for the treatment of intracranial atheromatous disease: periprocedural results. *Stroke*. 2007;38:881–887.
82. Levy EI, Turk AS, Albuquerque FC, Niemann DB, Aagaard-Kienitz B, Pride L, Purdy P, Welch B, Woo H, Rasmussen PA, Hopkins LN, Masaryk TJ, McDougall CG, Fiorella DJ. Wingspan in-stent restenosis and thrombosis: incidence, clinical presentation, and management. *Neurosurgery*. 2007;61:644–650.
83. Zaidat OO, Klucznik R, Alexander MJ, Chaloupka J, Lutsep H, Barnwell S, Mawad M, Lane B, Lynn MJ, Chimowitz M; NIH Multicenter Wingspan Intracranial Stent Registry Study Group. The NIH registry on use of the Wingspan stent for symptomatic 70–99% intracranial arterial stenosis. *Neurology*. 2008;70:1518–1524.
84. Chimowitz MI. Intracranial stents for arterial stenosis (grant number 5k24ns050307-03). Available at: http://crisp.Cit.Nih.Gov/crisp/crisp_lib.Getdoc?Textkey=7153508&p_grant_num=5k24ns050307-03&p_query=&ticket=42041844&p_audit_session_id=254805344&p_keywords=. Accessed August 8, 2007.
85. Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke*. 2006;37:577–617.
86. Tissue plasminogen activator for acute ischemic stroke: The National Institute of Neurological Disorders and Stroke rt-Pa Stroke Study Group. *N Engl J Med*. 1995;333:1581–1587.

87. Qureshi AI, Suri MF, Nasar A, He W, Kirmani JF, Divani AA, Prestigiacomo CJ, Low RB. Thrombolysis for ischemic stroke in the United States: data from National Hospital Discharge Survey 1999–2001. *Neurosurgery*. 2005;57:647–654.
88. Qureshi AI, Kirmani JF, Sayed MA, Siddiqui AM, Safdar A, Pande RU, Ahmed S, Ferguson R, Hershey LA, Qazi KJ. Buffalo metropolitan area and Erie County stroke study: rationale, design, and methods. *Neuroepidemiology*. 2004;23:289–298.
89. Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, Pessin M, Ahuja A, Callahan F, Clark WM, Silver F, Rivera F. Intra-arterial prourokinase for acute ischemic stroke: the PROACT II study: a randomized controlled trial: Prolyse in Acute Cerebral Thromboembolism. *JAMA*. 1999;282:2003–2011.
90. Saqqur M, Molina CA, Salam A, Siddiqui M, Ribo M, Uchino K, Calleja S, Garami Z, Khan K, Akhtar N, O'Rourke F, Shuaib A, Demchuk AM, Alexandrov AV; CLOTBUST Investigators. Clinical deterioration after intravenous recombinant tissue plasminogen activator treatment: a multicenter transcranial Doppler study. *Stroke*. 2007;38:69–74.
91. Mandava P, Kent TA. Intra-arterial therapies for acute ischemic stroke. *Neurology*. 2007;68:2132–2139.
92. Schellinger PD, Hacke W. Intra-arterial thrombolysis is the treatment of choice for basilar thrombosis: pro. *Stroke*. 2006;37:2436–2437.
93. Ford GA. Intra-arterial thrombolysis is the treatment of choice for basilar thrombosis: con. *Stroke*. 2006;37:2438–2439.
94. Powers WJ. Intra-arterial thrombolysis for basilar artery thrombosis: trial it. *Stroke*. 2007;38:704–706.
95. Smith WS. Intra-arterial thrombolytic therapy for acute basilar occlusion: pro. *Stroke*. 2007;38:701–703.
96. del Zoppo GJ, Higashida RT, Furlan AJ, Pessin MS, Rowley HA, Gent M. PROACT: a phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke: PROACT Investigators: Prolyse in Acute Cerebral Thromboembolism. *Stroke*. 1998;29:4–11.
97. Ducrocq X, Bracard S, Taillandier L, Anxionnat R, Lacour JC, Guillemin F, Debouverie M, Bollaert PE. Comparison of intravenous and intra-arterial urokinase thrombolysis for acute ischaemic stroke. *J Neuroradiol*. 2005;32:26–32.
98. Inoue T, Kimura K, Minematsu K, Yamaguchi T; Japan Multicenter Stroke Investigator's Collaboration. A case-control analysis of intra-arterial urokinase thrombolysis in acute cardioembolic stroke. *Cerebrovasc Dis*. 2005;19:225–228.
99. Macleod MR, Davis SM, Mitchell PJ, Gerraty RP, Fitt G, Hankey GJ, Stewart-Wynne EG, Rosen D, McNeil JJ, Bladin CF, Chambers BR, Herkes GK, Young D, Donnan GA. Results of a multicentre, randomised controlled trial of intra-arterial urokinase in the treatment of acute posterior circulation ischaemic stroke. *Cerebrovasc Dis*. 2005;20:12–17.
100. Qureshi AI, Siddiqui AM, Kim SH, Hanel RA, Xavier AR, Kirmani JF, Suri MF, Boulos AS, Hopkins LN. Reocclusion of recanalized arteries during intra-arterial thrombolysis for acute ischemic stroke. *AJNR Am J Neuroradiol*. 2004;25:322–328.
101. Adams HP Jr, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, Grubb RL, Higashida RT, Jauch EC, Kidwell C, Lyden PD, Morgenstern LB, Qureshi AI, Rosenwasser RH, Scott PA, Wijdicks EF. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists [published corrections appear in *Stroke*. 2007;38:e38 and 2007;38:e96]. *Stroke*. 2007;38:1655–1711.
102. Qureshi AI, Kirmani JF, Siddiqui AM, Hanel RA, Kim SH, Hopkins LN. Outcomes in acute ischemic stroke patients without angiographically documented arterial occlusion. *J Neuroimaging*. 2005;15:37–42.
103. del Zoppo GJ, Poeck K, Pessin MS, Wolpert SM, Furlan AJ, Ferbert A, Alberts MJ, Zivin JA, Wechsler L, Busse O, Greenlee R Jr, Brass L, Mohr JP, Feldmann E, Hacke W, Kase CS, Biller J, Gress D, Otis SM. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. *Ann Neurol*. 1992;32:78–86.
104. Tomsick TA. Intravenous thrombolysis for acute ischemic stroke. *J Vasc Interv Radiol*. 2004;15:S67–S76.
105. Lewandowski CA, Frankel M, Tomsick TA, Broderick J, Frey J, Clark W, Starkman S, Grotta J, Spilker J, Khoury J, Brott T. Combined intravenous and intra-arterial r-TPA versus intra-arterial therapy of acute ischemic stroke: Emergency Management of Stroke (EMS) Bridging Trial. *Stroke*. 1999;30:2598–2605.
106. IMS Study Investigators. Combined intravenous and intra-arterial recanalization for acute ischemic stroke: the Interventional Management of Stroke Study. *Stroke*. 2004;35:904–911.
107. Tomsick T, Broderick J, Carrozella J, Khatri P, Hill M, Palesch Y, Khoury J; Interventional Management of Stroke II Investigators. Revascularization results in the Interventional Management of Stroke II trial. *AJNR Am J Neuroradiol*. 2008;29:582–587.
108. IMS III. Interventional Management of Stroke (IMS) III trial Web page. Available at: http://clinicaltrials.Gov/ct2/show/nct00359424?Term=interventional+stroke+trial&rank=1. Accessed May 28, 2008.
109. Higashida RT, Furlan AJ, Roberts H, Tomsick T, Connors B, Barr J, Dillon W, Warach S, Broderick J, Tilley B, Sacks D; Technology Assessment Committee of the American Society of Interventional and Therapeutic Neuroradiology; Technology Assessment Committee of the Society of Interventional Radiology. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke [published correction appears in *Stroke*. 2003;34:2774]. *Stroke*. 2003;34:e109–e137.
110. Schumacher HC, Meyers PM, Yavagal DR, Harel NY, Elkind MS, Mohr JP, Pile-Spellman J. Endovascular mechanical thrombectomy of an occluded superior division branch of the left MCA for acute cardioembolic stroke. *Cardiovasc Intervent Radiol*. 2003;26:305–308.
111. Yu W, Binder D, Foster-Barber A, Malek R, Smith WS, Higashida RT. Endovascular embolectomy of acute basilar artery occlusion. *Neurology*. 2003;61:1421–1423.
112. Gobin YP, Starkman S, Duckwiler GR, Grobelny T, Kidwell CS, Jahan R, Pile-Spellman J, Segal A, Vinuela F, Saver JL. MERCI 1: a phase 1 study of Mechanical Embolus Removal in Cerebral Ischemia. *Stroke*. 2004;35:2848–2854.
113. Smith WS, Sung G, Saver J, Budzik R, Duckwiler G, Liebeskind DS, Lutsep HL, Rymer MM, Higashida RT, Starkman S, Gobin YP, Frei D, Grobelny T, Hellinger F, Huddle D, Kidwell C, Koroshetz W, Marks M, Nesbit G, Silverman IE; Multi MERCI Investigators. Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI trial. *Stroke*. 2008;39:1205–1212.
114. Phatouros CC, Higashida RT, Malek AM, Smith WS, Mully TW, DeArmond SJ, Dowd CF, Halbach VV. Endovascular stenting of an acutely thrombosed basilar artery: technical case report and review of the literature. *Neurosurgery*. 1999;44:667–673.
115. Nakano S, Iseda T, Yoneyama T, Kawano H, Wakisaka S. Direct percutaneous transluminal angioplasty for acute middle cerebral artery trunk occlusion: an alternative option to intra-arterial thrombolysis. *Stroke*. 2002;33:2872–2876.
116. Nakano S, Wakisaka S. Mechanical recanalization for acute ischemic stroke. *Neurocrit Care*. 2004;1:379–383.
117. Levy EI, Ecker RD, Horowitz MB, Gupta R, Hanel RA, Sauvageau E, Jovin TG, Guterman LR, Hopkins LN. Stent-assisted intracranial recanalization for acute stroke: early results. *Neurosurgery*. 2006;58:458–463.
118. Jovin TG, Gupta R, Uchino K, Jungreis CA, Wechsler LR, Hammer MD, Tayal A, Horowitz MB. Emergent stenting of extracranial internal carotid artery occlusion in acute stroke has a high revascularization rate. *Stroke*. 2005;36:2426–2430.
119. Brekenfeld C, Remonda L, Nedeltchev K, v Bredow F, Ozdoba C, Wiest R, Arnold M, Mattle HP, Schroth G. Endovascular neuroradiological treatment of acute ischemic stroke: techniques and results in 350 patients. *Neurol Res*. 2005;27(suppl 1):S29–S35.
120. Gupta R, Vora NA, Horowitz MB, Tayal AH, Hammer MD, Uchino K, Levy EI, Wechsler LR, Jovin TG. Multimodal reperfusion therapy for acute ischemic stroke: factors predicting vessel recanalization. *Stroke*. 2006;37:986–990.
121. Janjua N, Qureshi AI, Kirmani J, Pullicino P. Stent-supported angioplasty for acute stroke caused by carotid dissection. *Neurocrit Care*. 2006;4:47–53.
122. Stapf C, Mast H, Sciacca RR, Berenstein A, Nelson PK, Gobin YP, Pile-Spellman J, Mohr JP; New York Islands AVM Study Investigators. The New York Islands AVM Study: design, study progress, and initial results. *Stroke*. 2003;34:e29–e33.
123. Jessurun GA, Kamphuis DJ, van der Zande FH, Nossent JC. Cerebral arteriovenous malformations in the Netherlands Antilles: high prev-

alence of hereditary hemorrhagic telangiectasia-related single and multiple cerebral arteriovenous malformations. *Clin Neurol Neurosurg*. 1993;95:193–198.
124. Brown RD Jr, Wiebers DO, Torner JC, O'Fallon WM. Incidence and prevalence of intracranial vascular malformations in Olmsted County, Minnesota, 1965 to 1992. *Neurology*. 1996;46:949–952.
125. Berman MF, Sciacca RR, Pile-Spellman J, Stapf C, Connolly ES Jr, Mohr JP, Young WL. The epidemiology of brain arteriovenous malformations. *Neurosurgery*. 2000;47:389–396.
126. Stapf C, Mohr JP, Pile-Spellman J, Solomon RA, Sacco RL, Connolly ES Jr. Epidemiology and natural history of arteriovenous malformations. *Neurosurg Focus*. 2001;11:e1.
127. Ogilvy CS, Stieg PE, Awad I, Brown RD Jr, Kondziolka D, Rosenwasser R, Young WL, Hademenos G. AHA scientific statement: recommendations for the management of intracranial arteriovenous malformations: a statement for healthcare professionals from a special writing group of the Stroke Council, American Stroke Association. *Stroke*. 2001;32:1458–1471.
128. Hartmann A, Mast H, Choi JH, Stapf C, Mohr JP. Treatment of arteriovenous malformations of the brain. *Curr Neurol Neurosci Rep*. 2007;7:28–34.
129. Brown RD Jr, Wiebers DO, Torner JC, O'Fallon WM. Frequency of intracranial hemorrhage as a presenting symptom and subtype analysis: a population-based study of intracranial vascular malformations in Olmsted Country, Minnesota. *J Neurosurg*. 1996;85:29–32.
130. Stapf C, Mast H, Sciacca RR, Choi JH, Khaw AV, Connolly ES, Pile-Spellman J, Mohr JP. Predictors of hemorrhage in patients with untreated brain arteriovenous malformation. *Neurology*. 2006;66:1350–1355.
131. Hartmann A, Pile-Spellman J, Stapf C, Sciacca RR, Faulstich A, Mohr JP, Schumacher HC, Mast H. Risk of endovascular treatment of brain arteriovenous malformations. *Stroke*. 2002;33:1816–1820.
132. Ledezma CJ, Hoh BL, Carter BS, Pryor JC, Putman CM, Ogilvy CS. Complications of cerebral arteriovenous malformation embolization: multivariate analysis of predictive factors. *Neurosurgery*. 2006;58:602–611.
133. Newton TH, Cronqvist S. Involvement of dural arteries in intracranial arteriovenous malformations. *Radiology*. 1969;93:1071–1078.
134. Meyers PM, Halbach VV, Phatouros CP, Dowd CF, Malek AM, Lempert TE, Lefler JE, Higashida RT. Hemorrhagic complications in vein of Galen malformations. *Ann Neurol*. 2000;47:748–755.
135. Johnston IH, Whittle IR, Besser M, Morgan MK. Vein of Galen malformation: diagnosis and management. *Neurosurgery*. 1987;20:747–758.

KEY WORDS: AHA Scientific Statments ■ aneurysm ■ aneurysm, intracranial ■ stroke ■ arteriovenous malformation, cerebral ■ circulation, cerebrovascular ■ practice guideline

Indications for the Performance of Intracranial Endovascular Neurointerventional Procedures: A Scientific Statement From the American Heart Association Council on Cardiovascular Radiology and Intervention, Stroke Council, Council on Cardiovascular Surgery and Anesthesia, Interdisciplinary Council on Peripheral Vascular Disease, and Interdisciplinary Council on Quality of Care and Outcomes Research

Philip M. Meyers, H. Christian Schumacher, Randall T. Higashida, Stanley L. Barnwell, Mark A. Creager, Rishi Gupta, Cameron G. McDougall, Dilip K. Pandey, David Sacks and Lawrence R. Wechsler

Circulation. 2009;119:2235-2249; originally published online April 6, 2009;
doi: 10.1161/CIRCULATIONAHA.109.192217
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539