

Reporting Standards for Angioplasty and Stent-assisted Angioplasty for Intracranial Atherosclerosis

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BACKGROUND AND PURPOSE: Intracranial cerebral atherosclerosis causes ischemic stroke in a significant number of patients. Technological advances over the past 10 years have enabled endovascular treatment of intracranial atherosclerotic stenosis. The number of patients treated with angioplasty or stent-assisted angioplasty for this condition is increasing. Given the lack of universally accepted definitions, the goal of this document is to provide consensus recommendations for reporting standards, terminology, and written definitions when reporting clinical and radiological evaluation, technique, and outcome of endovascular treatment using angioplasty or stent-assisted angioplasty for stenotic and occlusive intracranial atherosclerosis.

SUMMARY OF REPORT: This article was written under the auspices of Joint Writing Group of the Technology Assessment Committee, Society of NeuroInterventional Surgery, Society of Interventional Radiology; Joint Section on Cerebrovascular Neurosurgery of the American Association of Neurological Surgeons and Congress of Neurological Surgeons; and the Section of Stroke and Interventional Neurology of the American Academy of Neurology. A computerized search of the National Library of Medicine database of literature (PubMed) from January 1997 to December 2007 was conducted with the goal to identify published endovascular cerebrovascular interventional data in stenotic intracranial atherosclerosis that could be used as benchmarks for quality assessment. We sought to identify those risk adjustment variables that affect the likelihood of success and complications. This document offers the rationale for different clinical and technical considerations that may be important during the design of clinical trials for endovascular treatment of intracranial stenotic and occlusive atherosclerosis. Included in this guidance document are suggestions for uniform reporting standards for such trials. These definitions and standards are primarily intended for research purposes; however, they should also be helpful in clinical practice and applicable to all publications.

CONCLUSION: In summary, the definitions proposed represent recommendations for constructing useful research data sets. The intent is to facilitate production of scientifically rigorous results capable of reliable comparisons between and among similar studies. In some cases, the definitions contained here are recommended by consensus of a panel of experts in this writing group for consistency in reporting and publication. These definitions should allow different groups to publish results that are directly comparable.

J Vasc Interv Radiol 2009; 20:S451–S473

Key Words: anatomy, angiography, interventional neuroradiology, neuroradiology, reporting standard, reporting terminology, stenting

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Published in *Stroke*. 2009;40(5):e348–e365.

Published online before print February 26, 2009, doi: 10.1161/STROKEAHA.108.527580.

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DOI: 10.1016/j.jvir.2009.03.005

THE goal of this writing group is to provide consensus recommendations for the arteriographic evaluation and endovascular treatment of intracranial atherosclerosis. These criteria are aimed to design clinical trials, to provide uniformity of definitions for appropriate selection and stratification of patients, and to allow analysis and meta-analysis of reported data. This document must not be construed as defining standard-of-care. However, these reporting standards are intended for use in research protocols rather than for quality assessment in individual practice. These definitions represent one set of consensus recommen-

dations for constructing useful research data sets. These definitions do not represent the only data that are important or useful in the design of clinical trials, and they do not represent minimally acceptable data.

The intent is to facilitate production of scientifically rigorous results capable of reliable comparisons between and among similar studies. In some cases, the prescribed definitions contained here are arbitrary or operational but have been recommended by consensus of this writing group for consistency in reporting and publication.

BACKGROUND

Intracranial cerebral atherosclerosis causes ischemic stroke in a significant number of patients. In the United States, it is estimated that 40 000 to 60 000 first-ever and recurrent strokes are caused by intracranial cerebral atherosclerosis annually. Typical risk factors are insulin-dependent diabetes mellitus, hypertension, smoking, and hypercholesterolemia. The pathology of intracranial atherosclerosis is similar to other vascular territories (1). There seems to be a racial preference for this disorder affecting Asian, black, and Hispanic patients more often compared with whites. Medical primary and secondary stroke prevention in patients with intracranial cerebral atherosclerosis is often unsatisfactory. Technological advances over the past 10 years enabled endovascular treatment of intracranial atherosclerotic stenosis. The number of patients treated with angioplasty or stent-assisted angioplasty for intracranial stenosis is increasing. At present, the value of endovascular treatment for intracranial atherosclerosis has been demonstrated only in case series rather than in well-designed, randomized, controlled trials. There are only 2 prospective feasibility and safety trials using endovascular treatment of stenotic intracranial atherosclerosis (2,3). Based on this experience, the Society of Neurointerventional Surgery, Society of Interventional Radiology, and American Society of Neuroradiology recommended in 2005 angioplasty with or without stenting of a symptomatic patient with an intracranial stenosis of >50% who failed medical treatment (4). However, this recommendation is

not based on a well-designed, prospective, randomized Phase 3 trial comparing stent-assisted revascularization with best medical treatment of stenotic intracranial atherosclerosis. Based on current evidence, patients with symptomatic intracranial atherosclerosis may be considered for stent-assisted angioplasty on a compassionate-use basis or be enrolled in the Stenting versus Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis Trial, the ongoing National Institute of Neurological Diseases and Stroke-funded randomized clinical trial (5).

METHODS AND MATERIALS

Purpose

It is the purpose of this document to review indications and reporting of cerebral endovascular treatment procedures for stenotic intracranial atherosclerosis. This document includes currently available scientific data on endovascular cerebrovascular procedures for this disease entity. The document may therefore be useful at the institutional level: (1) to characterize the expected success and complication rates for neurovascular interventional procedures when performed by highly skilled operators; and (2) to develop recommendations for standards to assess operator proficiency and institutional program quality. These include standards for data collection to permit monitoring of appropriateness and effectiveness of neurovascular procedures for stenotic intracranial atherosclerosis both at the level of the operator and the institution.

Writing Group Composition

The writing group was selected to represent a broad range of experience, perspective, and expertise on neurovascular disease and treatment. The members of the writing group were identified on the basis of one or more of the following attributes: neurointerventionalists with a broad range of experience (in practice and in academic settings); individuals who have performed clinical research studying the outcome of neurovascular procedures and stroke; individuals who direct neuroendovascular training and treatment programs with a broad cross-section of interventional operators;

and individuals with broad clinical experience who have had considerable previous involvement with neurovascular procedures. No individual was refused participation in the project.

Literature Review

A computerized search of the National Library of Medicine database of literature (PubMed) from January 1997 to December 2007 was conducted with the goal to identify published endovascular cerebrovascular interventional data in stenotic intracranial atherosclerosis 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.

Broad key word phrases, including "intracranial atherosclerosis," "intracranial stenosis," "stroke," "transient ischemic attacks," "TIA," or "cerebral stenosis," were used in conjunction with procedural terms, including "intracranial stent," "intracranial angioplasty," "intracranial stent-assisted angioplasty," "thrombolysis," "intervention," "endovascular revascularization," and "endovascular treatment."

English and non-English language articles published between January 1, 1997, and December 31, 2007, are included. To identify further published, unpublished, and ongoing trials, reference lists of relevant articles were searched. Abstracts were reviewed and articles unrelated to the specific topic were excluded by the first author. Duplicate references and redundant publications were discarded by the first author. To have more reliable outcome data, we excluded case series with 7 or fewer patients.

Description of the patient population.—Symptomatic patients may present clinically with transient ischemic attacks, ischemic stroke, or both. Currently, there is insufficient evidence to recommend endovascular treatment for the asymptomatic patient (4,6).

Clinical Assessment of Comorbid Conditions and Functional Status

Description of the cardiovascular risk factors and functional status before any intervention is essential (Table 1). These include listing of classical cardiovascular risk factors such as age, gender, race and ethnicity, hyperten-

Table 1
Suggested Reporting of Baseline Characteristics of the Study Population

Age, Years	Mean ± SD
Gender, no. (%)	Female, male
Race, no. (%)	White, black, Hispanic, Asian
History of hypertension, no. (%)	
History of diabetes, no. (%)	
History of lipid disorder, no. (%)	
History of coronary artery disease, no. (%)	Myocardial infarction, angina
History of atrial fibrillation, no. (%)	
History of peripheral vascular disease, no. (%)	
Functional status prior to intervention (Barthel Index, Functional Independence Scale, mRS)	Mean ± SD
Stroke severity before intervention (NIHSS)	Mean ± SD
Smoking status, no. (%)	
Qualitative assessment	Never, previously, currently
Quantitative (pack-years of smoking)	Mean ± SD
History of ischemic stroke, no. (%)	
Qualifying event attributed to index artery	
Transient ischemic attack, no. (%)	
Ischemic stroke, no. (%)	
Blood pressure before intervention, mm Hg	
Systolic	Mean ± SD
Diastolic	Mean ± SD
Glycosylated hemoglobin before intervention, %	Mean ± SD
Cholesterol, mg/dL or mmol/L	
High-density lipoprotein	Mean ± SD
Low-density lipoprotein	Mean ± SD
Use of antithrombotic treatment at qualifying event, no. (%)	
Type and dose of antithrombotic treatment at qualifying event, no. (%)	Aspirin, clopidogrel, aspirin/extended-release dipyridamole, ticlopidine, Coumadin, phenprocoumon, combination therapy of either drug
Time from qualifying event to endovascular intervention, days	Mean ± SD
Type and dose of antithrombotic treatment at time of medical treatment failure, no. (%)	Aspirin, clopidogrel, aspirin/extended release dipyridamole, ticlopidine, intravenous unfractionated heparin, heparinoid, Coumadin, phenprocoumon, combination therapy of either drug
Type and dose of statin treatment at qualifying event, no. (%)	
Type and dose of statin treatment at time of medical treatment failure, no. (%)	
Type and dose of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker at qualifying event, no. (%)	
Type and dose of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker at time of medical treatment failure, no. (%)	
Type and dose of diuretic treatment at qualifying event, no. (%)	
Type and dose of diuretic treatment at time of medical treatment failure, no. (%)	

sion, hyperlipidemia, diabetes, or smoking and may also include more recently identified risk factors for cardiovascular disease such as C-reactive protein or homocysteine levels. Comorbid conditions are important because they affect outcome. The most common comorbidities are cardiac, pulmonary, and renal disease. The

functional status of the patient before the procedure must be reported using appropriately validated assessment tools and measurement scales. Widely used measures for disability and activities of daily living are the Barthel Index (7), Functional Independence Scale (8), and the modified Rankin Scale (mRS) (9). The severity of any

neurological deficit at any point in time before or after the intervention should be assessed by the National Institutes of Health Stroke Scale (NIHSS) (10) with or without another, similar acute stroke scale. A detailed listing of various scales used in stroke outcome trials can be found at the Internet Stroke Center (11). Investigators using

either of these scales should have been trained, tested, and certified in their use to assure their correct application (12–14).

Patient Selection According to Underlying Pathophysiology of Brain Ischemia Secondary to Intracranial Atherosclerosis

Transient ischemic attacks or ischemic stroke secondary to intracranial cerebral atherosclerosis are caused by 4 proposed different mechanisms. These mechanisms are not mutually exclusive: (1) perfusion failure secondary to stenosis and poor collateral circulation (15,16); (2) thrombosis at the site of stenosis secondary to a complicated atherosclerotic plaque (rupture, hemorrhage into the plaque, or occlusive plaque growth) (17–21); (3) thromboembolic events distal to the stenosis (22–27); and (4) direct occlusion of a penetrating artery at the site of the plaque (19,28–32).

Identification of a potential candidate for endovascular treatment requires appropriate clinical evaluation. This may be accomplished through a team approach by vascular neurologists, neuroendovascular specialists, neuroanesthesiologists, and, if available, neurointensivists. This team should evaluate all patients to correlate the patient's symptoms and clinical findings with the presumed symptomatic vessel and to exclude other potential diagnoses with alternative treatment options, for example, cerebral vasculitis or moyamoya disease. Part of this evaluation should include type and duration of medical therapy with adjustment of medical treatment as necessary. At present, intervention is generally considered only after failure of adequate medical therapy.

The most appropriate candidates for endovascular treatment are those with symptomatic perfusion failure. The presence of ischemic lesions in the white matter border zone territories of major cerebral arteries suggests perfusion failure. For example, in hemispheric disease due to middle cerebral artery stenosis, this may be apparent on brain imaging as nonconfluent or confluent ischemic lesions in the ipsilateral supra- or paraventricular white matter (33). Analysis of the clinical syndrome and the results of neuroimaging must be performed to exclude patients with symptomatic penetrating artery disease at the site of the stenosis (Group 4 specified previ-

ously). Patients with symptomatic penetrating artery disease may not benefit from endovascular treatment or even become further harmed by its application.

Patients with suspected cerebrovascular disease are often evaluated by transcranial Doppler or Duplex sonography, CT angiography, or MRI with MR angiography. Intracranial stenoses in the arteries accessible to angioplasty and stenting can be identified with any of those studies. In general, sensitivity and specificity with these noninvasive studies is lower compared with standard catheter-based angiography (see the "Measurement of the Grade of Individual Intracranial Atherosclerotic Lesions" section for details on stenosis assessment) (34–40). Impaired cerebrovascular reserve as an indicator for perfusion failure distal to the stenosis is diagnosed by several methods, each of them having its own advantages and disadvantages (41). Cerebral blood flow can be evaluated at baseline and after a cerebral vasodilatory stimulus such as hypercapnia or acetazolamide. In the normal situation, each of those stimuli results in an increase of cerebral blood flow. If the cerebral blood flow response is muted or absent, pre-existing cerebral vasodilatation due to reduced cerebral perfusion pressure is assumed. Measurements of cerebral blood flow can be made by several methods, including ^{133}Xe by inhalation or intravenous injection, single photon emission CT, stable xenon CT, positron emission tomography, CT and MRI-perfusion studies after the injection of an adequate contrast medium (41–47). Changes in flow velocity as determined by transcranial Doppler and CO_2 inhalation as compared with baseline also serve to estimate reduced poststenotic vasoreactivity. However, for technical reasons, all of these techniques allow only the diagnosis of Stage 1 of hemodynamic compromise (autoregulatory vasodilation), which is characterized by increased cerebral blood volume or mean vascular transit time distal to the stenosis. At the present time, the diagnosis of Stage 2 hemodynamic compromise (autoregulatory failure), which is characterized by decreased cerebral blood volume and increased oxygen extraction fraction, is only possible with positron

emission tomography using O^{15} -labeled radiotracers (41).

Description of Medical Treatment Failure before Endovascular Treatment

In the absence of proven efficacy of endovascular revascularization by appropriately designed randomized trials over medical treatment, most endovascular interventions are performed in patients who have failed maximal medical treatment. There remains no unique definition for the term "maximal medical treatment." Most vascular specialists use it when a patient continues to have cerebrovascular ischemic events in the territory of the affected intracranial cerebral artery despite optimal management of modifiable cardiovascular risk factors and anticoagulant or antiplatelet treatment for secondary stroke prevention. The time period from the initial cerebrovascular event to a subsequent cerebrovascular event in the territory of the index artery has not been uniquely established. There is evidence that some patients with symptomatic intracranial stenosis have a high rate of early treatment failure with medical treatment within the first few weeks of the initial event (48–50).

Timing of Endovascular Treatment after an Ischemic Stroke

Some patients referred for endovascular intracranial revascularization secondary to intracranial atherosclerosis will have had an ischemic stroke. Patients in the hyperacute or acute stage after an ischemic stroke may be more prone to revascularization-related complications compared with patients in the subacute or chronic phase (51). Therefore, timing of the endovascular intervention is critical in patients with ischemic strokes secondary to intracranial atherosclerosis (51). In Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYL-VIA), which evaluated the NeuroLink stent (Guidant, Inc, Indianapolis, Ind) for treatment of symptomatic intracranial atherosclerosis, patients were excluded if they had an ischemic stroke within 6 weeks before the procedure (2). In a recent trial using the Wing-Span Stent System with Gateway PTA Balloon Catheter (referred as Wing-Span Trial in the subsequent text), patients were considered for intracranial stenting at least 7 days after having an ischemic stroke (52), a time window

that is used by most endovascular surgeons. Because timing after ischemic stroke may influence outcome, the mean or median time from stroke to endovascular procedure needs to be reported.

Recommendation

A detailed description of the baseline characteristics of the patient (demographic data, cardiovascular risk factors, comorbidities, neurological status, functional status), type and duration of treatment before the endovascular intervention, and time in days from index event to intervention is recommended. In the absence of a uniquely accepted definition of "failure of maximal therapy," authors should provide detailed criteria about how "maximal medical therapy" is defined. Patients classified as failing medical therapy should have recurrent symptoms despite being on antithrombotic treatment (antiplatelet agents, oral or intravenous anticoagulation, or a combination of antiplatelet agents and anticoagulation). The underlying pathophysiology (perfusion failure, distal embolism, local thrombosis at the stenosis) of the symptomatic intracranial stenosis needs to be specified as well as the technique used to make that diagnosis before the intervention. In addition, duration of medical therapy before the procedure and the delay period between an ischemic stroke and endovascular procedure need to be reported.

Angiographic evaluation of intracranial atherosclerosis.—Measurement of the Grade of Individual Intracranial Atherosclerotic Lesions

Parent vessel diameter and length of the intracranial atherosclerotic stenosis is critical for optimal results in angioplasty or stent-assisted angioplasty. For example, the WingSpan system (Boston Scientific, Ind, Fremont, Calif) offers 15 different stents of various combinations of 3 different lengths (9, 15, and 20 mm) and 5 different diameters (2.5, 3.0, 3.5, 4.0, and 4.5 mm) (52,53). Accurate and precise measurement of the stenosis, its length, and normal vessel caliber adjacent to the stenosis are used to select appropriate balloon length and diameter. Patient motion artifact limits resolution, may require repeat angiographic sequences, and increases con-

trast load. The injured brain can be intolerant of smaller doses of iodinated contrast than the uninjured brain. Contrast dose should be limited to a maximum of 5 to 7 mg/kg even with good renal function. Length and diameter of the atherosclerotic lesion are typically measured on angiograms obtained with the lesion centered at the center of the detector to minimize distortion.

Appropriate calculations of the magnification factor need to be performed and may vary depending on the brand of angiographic equipment used (54). Catheter-based film-screen angiography cannot be used to perform distance measurements without reference markers of some type. However, using markers of known size (eg, washers, dimes, and so on) exacting measurements can be made. Standard digital subtraction angiography can be used to perform measurements, but errors are inherent in the system. Line pair resolution of film-screen angiography is potentially higher than that of digital angiography. Most angiographic systems using film-screen angiography do not have software to perform automated measurements. Techniques to obtain measurements using cut film angiography are well described but potentially fraught with error if not properly performed. Modern digital angiographic equipment uses sensors or makes assumptions about source-to-image distance (SID) to obtain distance measurements of 2-dimensional angiographic images. This equipment is supplied with software by the manufacturer allowing calculations of vessel diameter and stenosis grades with a calculated potential measurement error in the magnitude of 1.5%. Careful and frequent calibration for precision and accuracy are crucial to ensure patient safety.

The methods used for stenosis grading in the extracranial vessels such as the European Carotid Surgery Trialists' Collaborative (55,56) and North American Symptomatic Carotid Endarterectomy Trial criteria (57), are not suitable for intracranial vessels because of anatomic details intrinsic to this vascular territory, although previously used by some reporting endovascular specialists (58–61). Intracranial arteries are more tortuous, become narrower, and have multiple branch points. The Warfarin–Aspirin

Symptomatic Intracranial Disease Study (WASID) Group established a reliable method for measurement of stenosis grades in the intracranial major cerebral arteries (62). The stenosis grade is measured using the following equation:

$$\text{Stenosis (\%)} = \left[1 - \left(\frac{D_{\text{stenosis}}}{D_{\text{normal}}} \right) \right] \times 100$$

where D_{stenosis} is the diameter of the artery at the site of the most severe grade of stenosis and D_{normal} is the diameter of the proximal normal artery. For anatomic reasons, the diameter of the proximal normal artery is defined differently for the intracranial internal carotid artery as compared with the middle cerebral, intracranial vertebral, and basilar arteries:

1. Measurement of D_{normal} for stenoses located in the middle cerebral, intracranial vertebral, or basilar arteries:
 - a. If there is a focal stenosis not affecting the origin of otherwise normal index artery the widest, parallel, normal, proximal, nontortuous segment is chosen to measure D_{normal} (Figure 1).
 - b. If the index artery is stenotic at its origin and its feeding artery is normal, the widest, normal, nontortuous segment of the feeding artery is chosen to measure D_{normal} .
 - c. If the index artery is diseased in its entire length, the most distal, normal, parallel, nontortuous segment of the artery is chosen to measure D_{normal} .
2. Measurement of D_{normal} for stenoses in the intracranial carotid artery
 - a. For the precavernous, cavernous, and postcavernous intracranial carotid artery, the widest, nontortuous, normal portion of the petrous carotid artery is chosen to measure D_{normal} (Figure 2).
 - b. If the entire petrous portion of the carotid artery is diseased, the most distal, parallel, normal part of the extracranial internal carotid artery is chosen to measure D_{normal} .

Using this method, 3 raters achieved an intraobserver agreement of 81%

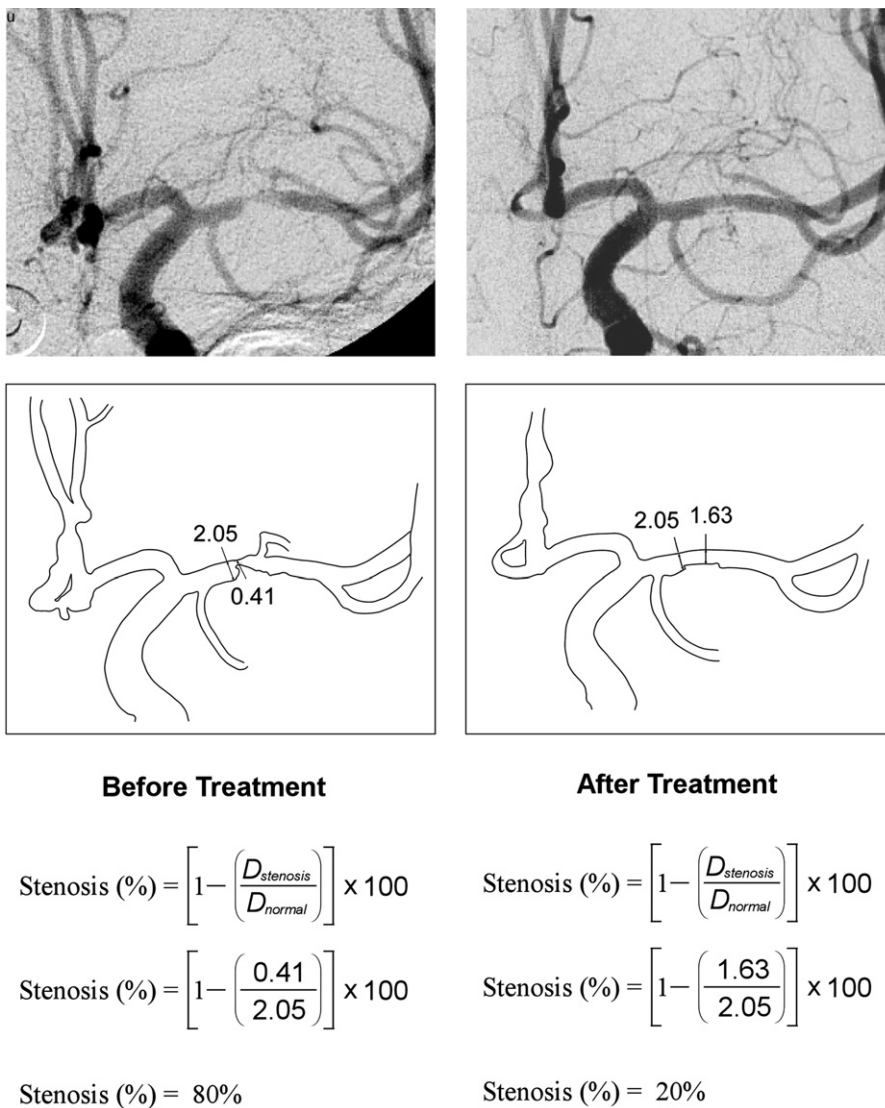


Figure 1. Measurement of stenoses located in the middle cerebral, intracranial vertebral, or basilar arteries. If there is a focal stenosis that does not involve the origin of index artery, then the widest, parallel, normal, proximal, nontortuous segment is chosen to measure the normal reference diameter (D_{normal}). If the index artery is stenotic at its origin, but its feeding artery is normal, the widest, normal, nontortuous segment of the feeding artery is chosen to measure D_{normal} . If the index artery is diseased in its entire length, the most distal, normal, parallel, nontortuous segment of the artery is chosen to measure D_{normal} .

and 100% and an interobserver agreement of 67% to 88%. Another method to estimate stenosis grades is based on comparison of the contralateral, non-diseased artery. This method is less reliable because there are normal caliber variations between paired vessels and this approach may lead to unacceptable over- or underestimation of the stenosis grade depending on which vessel is larger, the affected or nonaffected one. In rare cases, the ste-

nosis is so tight that accurate measurement of the stenosis grade is impossible. In this situation, some operators report the stenosis grade as 95% (63).

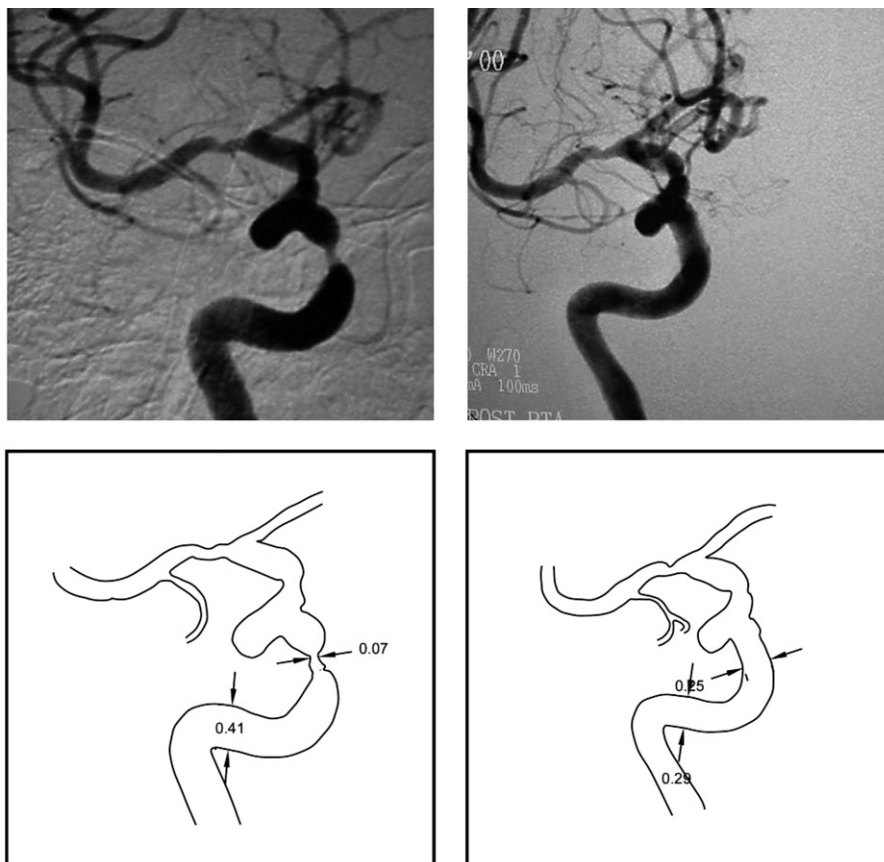
The mentioned methods to calculate the degree of stenosis are limited because of the pitfalls in choosing a denominator as a reference point. A promising new method in circumventing this limitation is direct measurement of arterial stenoses in millimeters, the numerator in the methods

used in North American Symptomatic Carotid Endarterectomy Trial, European Carotid Surgery Trialists' Collaborative, and WASID. For example, modern high-speed multidetector CT and CT angiography techniques (64–66) allow direct millimeter measurement of contrast-filled vessels and surrounding noncontrast-filled soft tissues. This technique of direct millimeter measurement is successfully used for stenosis grading of the extracranial carotid artery of severe stenoses ($\geq 70\%$) with a reported sensitivity of 88.2%, specificity of 92.4%, and negative predicted value of 98.2% (64). Similar measurements for direct stenosis measurement in millimeters can be performed with MR angiography or 3-dimensional digital subtraction angiography (67). The feasibility and accuracy of direct measurement of intracranial stenoses in millimeter needs to be established in large series. Direct measurement of intracranial stenoses in millimeters may prove to be a more accurate method compared with the method used in WASID.

Recommendation

Outcome studies critically rely on accurate measurements of stenosis grades before and after any intervention. The method developed by the WASID Study group to measure stenosis grade in intracranial arteries is recommended. If authors choose to use a different measurement system, it must be described in great detail. Either way, measurements should be performed by at least by 2 experienced raters independently. Intrarater and interrater variability for the measurements needs to be reported.

Extent and severity of intracranial atherosclerosis.—Mori et al (68,69) developed an arteriographic classification system predicting the outcome of cerebral revascularization with primary angioplasty. Lesions were categorized at high-resolution digital subtraction arteriography by length and geometry: Type A: short (≤ 5 mm in length), concentric or moderately eccentric, nonocclusive; Type B: tubular (5 to 10 mm in length), extremely eccentric, moderately angulated (curved); and Type C: diffuse (>10 mm in length),



Before Treatment

After Treatment

$$\text{Stenosis (\%)} = \left[1 - \left(\frac{D_{\text{stenosis}}}{D_{\text{normal}}} \right) \right] \times 100$$

$$\text{Stenosis (\%)} = \left[1 - \left(\frac{8.2}{48} \right) \right] \times 100$$

Stenosis (%) = 83%

Stenosis (%) = 14%

Figure 2. Measurement of stenoses in the intracranial carotid artery. For the precavernous, cavernous, and postcavernous intracranial carotid artery, the widest, nontortuous, normal portion of the petrous carotid artery is chosen to measure the normal reference diameter (D_{normal}). If the entire petrous portion of the carotid artery is diseased, the most distal, parallel, normal part of the extracranial internal carotid artery is chosen to measure D_{normal} .

extremely angulated (>90°), very tortuous proximal segment.

The more complex the target lesion, the less satisfactory immediate- and long-term outcomes become. Although this classification scheme was developed for angioplasty alone, it is now widely used also to describe lesions for stent-assisted angioplasty.

Jiang and coworkers proposed a classification of the location of the stenotic atheroma with respect to the bifurcation of the middle cerebral artery (70). They divided atheromata into Type A (prebifurcation lesion), Type B (postbifurcation lesion), Type C (lesion across the nonstenotic ostium of its branch), Type D (lesion across the

stenotic ostium of its branch), Type E (ostium lesion of branch alone), Type F (combined prebifurcation lesion and its small branch ostium), and Type N (nonbifurcation lesion). Depending on the patient's symptoms and collateral blood flow, Jiang and coworkers stratified placement of a stent across at the bifurcation of the middle cerebral artery-M1 segment. The usefulness of this classification remains to be established.

Recommendation

Outcome studies critically rely on the severity and extent of intracranial atherosclerosis and its description is important. Whichever classification is used should be readily explained and any ratings should be performed independently by at least 2 experienced observers. Intrarater and interrater variabilities for the severity of intracranial atherosclerosis need to be reported.

Treatment description.—Operator Experience

Operator experience is critical for success in any procedure. Intracranial angioplasty and stent-assisted angioplasty for intracranial atherosclerosis are fairly new procedures and even at tertiary referral centers, the number of treated cases annually is small in relation to other neurointerventional procedures, for example, extracranial carotid stenting (71). Currently, there is no widely accepted credentialing procedure specific to intracranial angioplasty or stent-assisted angioplasty comparable to endovascularization procedures for extracranial carotid arteries used in clinical trials (72–74). In a recent joint statement from the American Academy of Neurology, the American Association of Neurological Surgeons, the American Society of Interventional and Therapeutic Neuro-radiology, the American Society of Neuroradiology, the Congress of Neurological Surgeons, the American Association of Neurological Surgeons/Congress of Neurological Surgeons Cerebrovascular Section, and the Society of Interventional Radiology, the requirement of a defined formal training and experience in both the cognitive and technical aspects of the neurosciences for the performance and interpretation of diagnostic and therapeutic cervical and cerebrovascular procedures was deemed essential (75).

Based on this statement, intracranial angioplasty and stent-assisted angioplasty for intracranial atherosclerosis should only be performed by appropriately trained neurovascular interventionalists. A statement specifying neurovascular expertise as defined here needs to be reported.

Periprocedural Medical Therapy

In most cases, medical therapy immediately before intracranial revascularization must be adjusted. This adjustment is typically performed a few days before the endovascular intervention. Any periprocedural medical therapy may affect outcome or induce complications related to the procedure. The most common situations reported in case series on intracranial angioplasty or stent-assisted angioplasty are:

1. Patients on long-term anticoagulation may need to be switched to unfractionated intravenous heparin drip or low-molecular-weight heparin treatment. This switch may be associated with major hemorrhagic complications or with ischemic thromboembolic events in high-risk patients (76–79).
2. Patients with chronic renal failure will need intravenous hydration, n-acetylcysteine, or bicarbonate treatment before the intervention to reduce the risk of contrast-induced nephropathy (80,81).
3. To prevent periprocedural platelet emboli, patients are typically treated for a variable number of days before the procedure with a combination of enteric-coated acetylsalicylic acid and clopidogrel. The dosing of each antiplatelet agent varies from operator to operator, and there is no consensus on the safety, dosage, or drug combination. Acetylsalicylic acid is given between 81 and 325 mg daily, whereas clopidogrel dosages vary between 75 and 300 mg daily before the procedure. Patients with ischemic strokes before the intervention are prone to hemorrhagic complications, especially while on a combination with 2 antiplatelet agents (82).
4. Management of blood pressure medications in patients with critical intracranial stenoses and perfusion failure is important. For some patients, withholding of their regular

antihypertensive medications is sufficient to stabilize brain perfusion before the procedure. For others, intravenous vasopressors may be required to achieve sufficient brain perfusion until endovascular revascularization is performed.

5. Some operators report use of oral (60 mg) (83,84) or intravenous nimodipine (0.6 to 2.0 mg per hour) (70) days before or at the day of the intervention as a neuroprotective agent. Use of these agents in this manner remains unproven.

Detailed reporting of these adjunctive medical interventions, including timing and duration in relation to the revascularization procedure is considered periprocedural management and needs to be reported. Even if a preprocedural complication precludes performance of the revascularization, such cases must be reported in the treatment series as management failures. The most common periprocedural interventions like anticoagulation, use of glycoprotein IIb/IIIa inhibitors, and infusion of vasodilators are discussed in more detail subsequently.

Periprocedural Anticoagulation

Intra-arterial clot formation is a major concern during angiography and endovascular revascularization and may have disastrous consequences. For this reason, unfractionated heparin is administered by intermittent bolus or continuous infusion throughout the procedure after an initial intravenous bolus for example of 2000 (85), 3000 (70,86), 5000 (84,86–89), or 10 000 (90–93) units or at a weight-based bolus of 70 U/kg body weight given at the beginning of the procedure. For patients receiving continuous glycoprotein IIb/IIIa inhibitors, an initial heparin bolus is given at 50 U/kg body weight (94). Anticoagulation is monitored by activated clotting time. Reported activated clotting time target ranges during the procedure for intracranial revascularization range between 150 to 200 seconds (58), 200 to 250 seconds (59,95,96), 200 to 300 seconds (2), 250 to 300 seconds (87), 250 to 350 seconds (61,97), or 300 to 350 seconds (96). Intravenous heparinization is either stopped immediately (2,59,61) or maintained for up to 24 hours (58,61,83,87) or longer after the procedure,

depending on the individual patient (58,83,98–100). At the end of the procedure, heparin is typically not reversed.

Periprocedural Use of Glycoprotein IIb/IIIa Inhibitors

Cardiologists often use glycoprotein IIb/IIIa inhibitors such as abciximab during and after endovascular coronary interventions. For neuroradiological procedures, this group of agents has been associated with higher major hemorrhage complications, including symptomatic and fatal intracranial hemorrhage (101). The dosages needed for neuroradiological procedures are probably lower compared with those used in coronary interventions. Some neuroendovascular specialists use glycoprotein IIb/IIIa inhibitors as a rescue medication when intra-arterial clot formation is present, whereas others use them routinely (96). Typical dosages for abciximab for neurointerventional procedures is a bolus of 0.25 mg/kg body weight followed by 0.125 μ g/kg/min (96). Concomitant intravenous heparin is adjusted to maintain an activated clotting time of 200 to 250 seconds when abciximab is given (95,96).

Infusion of Vasodilators during the Procedure

The infusion of vasodilators in the proximal parent vessel at the beginning of the procedure or in the target vessel before crossing the stenosis has been described to prevent symptomatic catheter-induced vasospasm. Drugs used for this purpose are nitroglycerin (83) or isosorbide dinitrate (1.25 to 5.0 mg as a single bolus) (102,103). Other agents include calcium channel blockers such as nicardipine and verapamil as well as papaverine. It is important that any measurement of stenosis grade is performed before and after any intra-arterial infusion of vasodilators.

Periprocedural Blood Pressure Management

In a recent meta-analysis, the mean incidence of intracranial hemorrhage due to hyperperfusion syndrome after surgical carotid endarterectomy is approximately 1.3% (range, 0.2% to 12.6%) (104). This risk is increased by the presence of profound preoperative cerebral ischemia with impaired he-

modynamic reserve (105). Other reports examining the incidence of cerebral hyperperfusion syndrome using perioperative transcranial Doppler studies have reported rates of up to 9% (106,107). In a series of 140 patients undergoing cerebral revascularization procedures, the incidence of cerebral hyperperfusion was 5%, whereas the incidence of intracranial hemorrhage was 1.4%, but with 0% mortality (108). Because the clinical findings in cerebral hyperperfusion syndrome may be subtle, and ancillary investigations examining postprocedural cerebral blood flow such as brain perfusion CT, nuclear medicine single photon emission CT, xenon CT, and transcranial Doppler sonography are not often performed, one may expect a significant reporting bias that can skew the published data. Pre- and periprocedural blood pressure management is critical to lower the risk for hyperperfusion syndrome with its potentially devastating consequences (109).

Normal systemic blood pressure ("normotension") after a revascularization procedure often represents excessive blood pressure (effective "hypertension") for the susceptible cerebral circulation. Already a low resistance system, the brain can sustain severe barotrauma due to the loss of cerebrovascular tone and reactivity. In general, pharmacologically induced hypotension is required in these cases while taking into account comorbidities, which could be exacerbated by hypotension.

No or little information is provided in most patient series as how to monitor and manage systemic blood pressure before, during, and after the endovascular procedure (2,51,54,58–60, 63,68–70,83,85–89,91–93,97,98,100,103, 110–127). Some operators maintain the blood pressure in a normal to slightly hypertensive range (120 to 140 mm Hg) or slightly below normal for 24 hours (61,128). Others maintain the systolic blood pressure in the range of 120 to 140 mm Hg for 24 to 48 hours after the procedure using intravenous urapidil for hypertensive patients and plasma expander plus isotonic fluid in hypotensive patients to avoid the use of catecholamines (129). In patients with hyperperfusion syndrome, blood

pressure is maintained below 120 mm Hg (130).

Recommendation

A detailed description of operator expertise in neurovascular procedures in general and intracranial angioplasty and stenting in particular is required in the study presentation. This can best be achieved by stating if the participating interventionalist(s) is/are board-certified for neurovascular procedures by one of the major societies (for example, American Society of Interventional and Therapeutic Neuro-radiology, American Association of Neurological Surgeons, Congress of Neurological Surgeons, or similar). This information should include the total number of diagnostic and therapeutic interventional procedures and the overall number of intracranial angioplasty or stent-assisted angioplasty procedures performed by the operator. Furthermore, a description of periprocedural medical treatment is recommended. The description should include how long each of the medications was given before, during, and after the endovascular revascularization procedure.

Procedural anesthesia.—Each patient will need a detailed evaluation by a neuroanesthesiologist in advance of the procedure. Patients with cerebral perfusion failure will poorly tolerate periods of even mild relative hypotension such as those that frequently occur after induction. Blood pressure control during the procedure and immediately afterward is critical both for the avoidance of hypotension and the prevention of hypertension. The anesthesiologist should have a full complement of equipment during the procedure, not only the subset that is often provided for "off-site" or outside the conventional operating room cases. Angioplasty or stent-assisted angioplasty of cerebral arteries has been performed successfully under general anesthesia (2,54,59,61,70,83,84,87,113, 129) or local anesthesia (2,60,61,83,91, 96,97,114,119,131,132). General anesthesia has the advantage of maximal reduction of motion artifacts. Procedure times may be reduced using general anesthesia. The major disadvantage of general anesthesia is the inability to perform serial neurological examinations to detect new neurolog-

ical symptoms during the procedure as is possible when operating under local anesthesia. Basilar artery lesions should be treated under general anesthesia because occlusion of the artery during balloon inflation may result in loss of consciousness and apnea. Disadvantages of local anesthesia in intracranial angioplasty and stent placement are patient motion and pain control.

Endovascular technique.—Anatomic Considerations of Intracranial Arteries Relevant to the Endovascular Technique

Anatomic considerations are crucial for successful endovascular interventions. Cerebral arteries differ from other systemic muscular arteries, including coronary arteries in several respects:

1. In contrast to extracranial arteries, intracranial arteries lack an external elastic membrane and the outer most layer of the muscle cells represents the boundary between tunica media and tunica adventitia (133,134).
2. Cerebral arteries are smaller in diameter compared with proximal coronary arteries; the outer diameter of the proximal middle cerebral artery has been measured as 2.41 ± 0.41 mm (135) or 3.71 mm (range, 2.74 to 4.92 mm) (136). In comparison, the outer diameter in the left anterior descending coronary artery ranges from 4.5 ± 0.3 mm proximally to 2.5 ± 0.37 mm distally (137,138).
3. With minimal differences among middle cerebral, basilar, and vertebral arteries, intracranial arteries are significantly thinner (average wall thickness, 0.094 ± 0.030 mm) compared with coronary arteries (average wall thickness 0.87 ± 0.23 mm) of similar size (138). There is some minimal variation among middle cerebral, basilar, and vertebral arteries (139).
4. The tunica media is the dominating arterial wall component in intracranial arteries, whereas the tunica adventitia is very thin. The ratio of intima, media, and adventitia to total arterial wall thickness in cerebral arteries is 0.17 ± 0.03 , 0.52 ± 0.06 , and 0.31 ± 0.05 , respectively (139). By comparison, the corresponding ratios in the middle segment of the left anterior descending

- coronary artery is 0.27 ± 0.02 , 0.36 ± 0.03 , and 0.40 ± 0.03 , respectively (138).
5. Cerebral arteries fail at much lower stretching forces compared with other arteries because they are stiffer in circumferential and longitudinal direction (135,140,141).
 6. Because intracranial arteries are suspended in cerebrospinal fluid, there is little support from surrounding perivascular tissue by contrast with coronary arteries.
 7. Intracranial arteries are tethered by branching arteries, which may be invisible angiographically with sizes less than $250 \mu\text{m}$. Catastrophic subarachnoid hemorrhage may follow from manipulation-induced rupture of these delicate branches. Furthermore, these small branches may support functionally important brain structures, like the internal capsule or brain stem. Occlusion of these branches may lead to severe neurological deficits depending on the brain structure affected.
 8. The characteristic tortuosity of intracranial arteries makes endovascular navigation challenging.

For these reasons, intracranial arteries are more prone to vasospasm and to vessel rupture at much lower forces compared with coronary arteries of similar size.

Goal of Intracranial Angioplasty or Stent-assisted Angioplasty

The goal of intracranial angioplasty alone or stent-assisted angioplasty is to reverse the symptomatic stenosis leading to better perfusion of the brain tissue in the distribution of the stenotic artery. There is no generally accepted goal as to what degree the stenosis should be reversed after intracranial angioplasty or stent-assisted angioplasty. For example, in SSYLVA, technical success was defined as a stenosis grade $\leq 30\%$ postprocedure (2). In the US WingSpan Multi-center Registry, procedural success was defined as completion of Gateway balloon angioplasty and WingSpan stent placement across the target lesion despite the degree of residual stenosis or any complications related to the procedure (142). In this registry, the average stenosis was $43.5 \pm 18.1\%$ after angioplasty alone and $27.2 \pm 16.7\%$ after stent deployment. The postangioplasty steno-

sis grade defining technical success varies from $\leq 20\%$ residual stenosis (70), $\leq 30\%$ residual stenosis (96), but most commonly $\leq 50\%$ residual stenosis (2,54,58,60,68,94,119). A reasonable definition of technical success would be reduction of stenosis grade $\leq 50\%$.

Microcatheters and Guidewires for Navigation

Soft flow-directed catheters for distal catheterization of the tortuous cerebral arteries, as used for endovascular treatment of arteriovenous malformations, are not applicable for navigation across cerebrovascular stenoses. For that reason, all intracranial angioplasty requires guidewire navigation. Intracranial arteries are tortuous and located more distally from the orifice of the guiding catheter to the target lesion as compared with coronary arteries. This leads to a "bowstring" effect because additional pressure is required to advance the microcatheter over the guidewire and makes endovascular navigation comparatively challenging. In a typical intracranial procedure, an appropriate guide catheter is placed into the cervical carotid or vertebral artery. Using biplane road maps, the intracranial stenosis is traversed with a soft-tipped guidewire. Subsequently, a microcatheter is advanced across the lesion and correct intraluminal position is confirmed with a small volume of contrast injection. An exchange-length floppy-tipped hydrophilic guide wire is subsequently positioned with its tip sufficiently distal to the lesion to provide sufficient support for the stent catheter. In the typical situation, this requires the tip to be in the insular (M2) branches of the middle cerebral artery for M1–middle cerebral artery stenoses (114), P2 segments of the posterior cerebral artery for basilar artery stenoses (115) or M1 segment of the middle cerebral artery for intracranial internal carotid artery stenoses (143). The use of a microcatheter and soft microguidewire to cross the stenosis initially and then exchange the treatment device (balloon catheter or balloon-mounted stent) using the over-the-wire technique may be technically superior and preferable as compared with the primary crossing of the stenosis with the treatment device. This technique reduces the risk of catastrophic vessel dis-

section of the delicate cerebral arteries considerably.

Balloon Angioplasty

Balloon angioplasty was the dominating technique before stent-assisted angioplasty was made possible with the development of new stents. Until angioplasty devices specifically developed for intracranial application were available, angioplasty balloons for coronary interventions were used for intracranial stenoses. Angioplasty is typically performed using an undersized balloon and performed very slowly over several minutes. Tearing of the vessel must be avoided, and the aim is stenosis resolution of $\leq 50\%$ of the vessel because small increases of the vessel diameter result in large increases in perfusion. This principle differs significantly from the procedure performed to revascularize coronary or peripheral arteries. Technical details describing the evolution and rationale for the current technique for intracranial angioplasty have been described in detail previously (84).

Stent Placement

Initial experience with angioplasty alone exposes certain limitations, and stent-assisted intracranial angioplasty, either staged or primary, is performed preferentially by some operators compared with angioplasty alone. Stent-assisted angioplasty in peripheral, extracranial cerebral, and coronary circulation has been shown to have a superior safety and efficacy profile compared with balloon angioplasty alone. Stents limit vessel wall recoil and the extent of iatrogenic dissection by compressing the intimal flap that may develop during angioplasty. However, stenting can be more traumatic to the vessel wall compared with angioplasty alone and the metallic struts of a stent may actually perforate intracranial vessels.

In most published series, coronary stents were used off-label for intracranial application in carefully selected patient series. Recently, drug-eluting coronary stents have been successfully placed in intracranial arteries for stenotic lesions (119). SSYLVA (2) used the first specifically devised stent for intracranial applications, the NeuroLink System, but despite US Food and Drug Administration approval,

this device is commercially not available. A second device, the WingSpan Stent System with Gateway PTA Balloon Catheter, specifically designed for intracranial applications, was approved by the US Food and Drug Administration in 2005 (144) after completion of a safety and feasibility study (53). The major advantage of the WingSpan device is slow stent expansion over several weeks, thus minimizing the risk for vessel dissection and rupture. A third device, the Neuroform stent system, has been used for the treatment of intracranial atherosclerotic lesions (145).

Experience with drug-eluting stents for intracranial application is limited (119,120,146–148). Recent data from coronary revascularization studies using drug-eluting stents have raised safety concerns because of a small but significant increase in the rate of death and myocardial infarction in patients treated with these stents as compared with bare-metal coronary stents (149). The same phenomenon of delayed thrombosis may be observed for intracranial applications. In addition, patients harboring drug-eluting stents require longer treatment with a combination of aspirin and clopidogrel to prevent in-stent thrombosis compared with patients treated with bare-metal stents, which are typically only treated with this combination. After percutaneous coronary intervention (PCI), the current consensus of the American College of Chest Physicians recommends dual therapy for 12 months of aspirin (75–100 mg/d) plus clopidogrel (75 mg/d) over aspirin alone for bare metal stents. For patients undergoing PCI with drug-eluting stents, dual therapy with aspirin (75–100 mg/d) plus clopidogrel (75 mg/d) for at least 12 months is recommended. Beyond 1 year, continued treatment with aspirin plus clopidogrel indefinitely is suggested if no bleeding or other tolerability issues occur (150). The guidelines of the European Society of Cardiology recommends dual therapy with aspirin and clopidogrel after placement of a bare-metal stent for 3 to 4 weeks and for 6 to 12 months after placement of a drug-eluting stent (151). More recent evidence based on coronary stenting suggests that treat-

ment up to 24 months may be necessary to prevent delayed stent thrombosis in drug-eluting stents (152). Similar consensus recommendations for intracranial stenting do not exist. In SSYLIVIA, antiplatelet treatment after stenting was performed with aspirin (minimum 100 mg daily) for a minimum of 1 year and clopidogrel (75 mg daily) for at least 4 weeks (2). In the US Multicenter WingSpan Registry, patients were typically discharged on both aspirin (325 mg daily) and clopidogrel (75 mg daily). The dual antiplatelet regimen was maintained for a minimum of 4 weeks after the procedure, after which time patients remained on aspirin therapy (325 mg daily) (142).

Most patients considered for stent-assisted intracranial atherosclerosis will belong to the patient population studied in the Management of Atherothrombosis with Clopidogrel in High-risk patients with recent transient ischemic attack or ischemic stroke (MATCH) trial (82). MATCH was designed to test whether the combination of clopidogrel and aspirin was better than clopidogrel alone for the prevention of vascular events among patients with recent non-cardioembolic ischemic stroke or transient ischemic attack and at least one additional vascular risk factor. These patients considered to be of high-risk for recurrent ischemic cerebrovascular events were randomized to clopidogrel (75 mg daily) or a combination therapy with clopidogrel (75 mg daily) and aspirin (75 mg daily). In MATCH, the risk for major hemorrhage was significantly increased in the combination group compared with clopidogrel alone with a 1.3% absolute increase in life-threatening bleeding. The choice to use a drug-eluting stent requiring a prolonged dual antiplatelet therapy, therefore, may lead to hemorrhagic complications and surpass the benefit of prevention of in-stent thrombosis.

Recommendations

A detailed description of equipment (guidewires, angioplasty balloons, stents) and the endovascular technique used for intracranial revascularization should be reported.

Outcomes analysis.—Anatomic Outcome

Technical Success

Technical success is defined by successful angioplasty or stent-assisted angioplasty of intracranial stenoses without any complications such as periprocedural infarcts, vessel dissection, or vessel rupture. The postangioplasty stenosis grade defining technical success varies from $\leq 20\%$ residual stenosis (70), $\leq 30\%$ residual stenosis (96), but most commonly $\leq 50\%$ residual stenosis (2,54,58,60,68,94,119). Most importantly, technical success should be heralded by freedom from ipsilateral ischemic or hemorrhagic strokes in the distribution of the treated target stenosis.

Acute Arterial Occlusion

This is defined as the persistent occurrence of a new severely impaired flow within the target artery that requires acute rescue intervention by an unassigned treatment strategy. Classification of flow impairment in the target artery should follow the Thrombolysis in Myocardial Infarction (153) definition as adapted for angiographic cerebral blood flow (154). The proposed classification is as follows (155).

Grade 0: No perfusion. No antegrade flow beyond the point of occlusion;

Grade 1: Penetration with minimal perfusion. The contrast material passes beyond the area of obstruction but fails to opacify the entire cerebral bed distal to the obstruction for the duration of the angiographic run;

Grade 2: Partial perfusion. The contrast material passes beyond the obstruction and opacifies the arterial bed distal to the obstruction. However, the rate of entry of contrast into the vessel distal to the obstruction and/or its rate of clearance from the distal bed are perceptibly slower than its entry into and/or clearance from comparable areas not perfused by the previously occluded vessel, eg, the opposite cerebral artery or the arterial bed proximal to the obstruction;

Grade 2a: Only partial filling (less than two thirds) of the entire vascular territory is visualized;

Grade 2b: Complete filling of all of the expected vascular territory is visualized, but the filling is slower than normal; and

Table 2
Complication Rates for Intracranial Angioplasty with or without Stenting in Patient Series with at Least 8 Treated Patients
(Percentages Are Calculated per Patient and Not per No. of Vessels Treated)*

Author, Year	Patients, No. (No. of Stenoses)	Recruitment Period of Patients	Technical Success, N (%)	Ischemic Stroke/Acute Vessel Occlusion, N (%)
Callahan et al, 1997 (170)	15	N/A	15 (100)	1 (7)
Takis et al, 1997 (83)	10	3 years	8 (80)	4 (40)
Mori et al, 1998 (68)	42	4 years	33 (79)	2 (4.8)
Yokote et al, 1998 (58)	17	N/A	15 (88)	1 (6)
Alazzaz et al, 2000 (113)	16	5 years	15 (94)	2 (13)
Gomez et al, 2000 (115)	12	16 months	12 (100)	0 (0)
Mori et al, 2000 (103)	10	9 months	8 (80)	0 (0)
Nahser et al, 2000 (100)	20	2 years	20 (100)	2 (10)
Barakate et al, 2001 (171)	11	2 years	11 (100)	2 (18)
Levy et al, 2001 (117)	11	24 months	11 (100)	2 (18)
Ramee et al, 2001 (118)	15	N/A	14 (93)	0 (0)
Terada et al, 2001 (172)	45	N/A	44 (98)	3 (6.7)
Gress et al, 2002 (87)	25	14 years	25 (100)	5 (20)
Lee et al, 2002 (173)	10	4 years	10 (100)	0 (0)
Levy et al, 2002 (97)	8	35 months	7 (88)	1 (13)
Gupta et al, 2003 (51)	18	5 years	17 (94)	2 (11)
Zhang et al, 2003 (174)	48	24 months	46 (96)	2 (4.2)
SSYVIA, 2004 (2)	43	12 months	43 (100)	3 (7)
De Rochemont et al, 2004 (129)	16	19 months	15 (94)	0 (0)
Matsumaru et al, 2004 (175)	62	11.5 years	55 (86)	3 (4.8)
Liu et al, 2004 (176)	46	21 months	45 (98)	0 (0)
Kim et al, 2004 (54)	14	35 months	12 (86)	2 (17)
Boulos et al, 2005 (120)	13	N/A	0 (0)	0 (0)
Henkes et al, 2005 (88)	15	N/A	15 (100)	1 (7)
Kessler et al, 2005 (89)	16	N/A	13 (81)	1 (6)
Kim et al, 2005 (86)	17	4 years	17 (100)	2 (12)
Lee et al, 2005 (60)	17	63 months	16 (94)	9 (56)
Lylyk et al, 2005 (177)	106	9 years	104 (98)	7 (6.6)
Qureshi et al, 2005 (96)	24	1 year	20 (83)	2 (8)
Straube et al, 2005 (61)	12	1 year	11 (92)	0 (0)
Suh et al, 2005 (123)	35	10 years	34 (97)	1 (3)
Weber et al, 2005 (59)	21	3 years	21 (100)	3 (14)
Yoon et al, 2005 (125)	32	10 years	29 (91)	1 (3)
Yu et al, 2005 (126)	18	4 years	18 (100)	1 (6)
Abou-Chebl et al, 2005 (119) and 2006 (130)	46	N/A	46 (100)	4 (9)
Gupta et al, 2006 (147)	29	24 months	26 (90)	1 (3.5)
Marks et al, 2006 (63)	120	11.5 years	120 (100)	3 (2.5)
Qureshi et al, 2006 (148)	21	19 months	18 (85.7)	4 (19.5)
Terada et al, 2006 (128)	99	8 years	N/A	N/A
Fiorella et al, 2007 (142)	78	9 months	77 (99)	2 (2.6)
Jiang et al, 2007 (178)	213	57 months	203 (95.3)	17 (8.0)
WingSpan trial, 2007 (52,53)	45	10 months	44 (98)	1 (2.3)
Freitas et al, 2007 (179)	32	36 months	31 (97)	3 (9)
Fiorella et al, 2007 (180)	44 (47)	7 years	45 (96)	11 (25)

ICH indicates intracranial hemorrhage; SAH, subarachnoid hemorrhage; N/A, not available.

*References are excluded from the table if they were published before 1996, presented results in less than 8 treated patients, included intra- and extracranial revascularization procedures but did not present the outcome data separately for intra- and extracranial procedures, included conditions other than intracranial atherosclerosis, were published in abstract form only, and did not contain sufficient detail in complication reporting. To avoid double counting, only the most recent report from the same authors and centers are included if there was sufficient evidence for an overlap with prior publications from the same center.

Grade 3: Complete perfusion. Antegrade flow into the bed distal to the obstruction occurs as

promptly as into the obstruction and clearance of contrast material from the involved bed is as

rapid as from an uninvolved other bed of the same vessel or the opposite cerebral artery.

Intracranial Hemorrhage, ICH and SAH Combined, N (%)	Vessel Vasospasm, N (%)	Vessel Dissection, N (%)	Vessel Perforation or Rupture, N (%)	Combined Neurologic Morbidity and Mortality, N (%)	Death, N (%)
1 (7)	0 (0)	0 (0)	1 (7)	2 (13)	1 (7)
0 (0)	5 (50)	1 (10)	0 (0)	4 (40)	0 (0)
1 (2.4)	0 (0)	1 (2.4)	1 (2.4)	3 (7.1)	0 (0)
1 (6)	0 (0)	1 (6)	0 (0)	2 (12)	0 (0)
0 (0)	0 (0)	3 (19)	0 (0)	2 (13)	0 (0)
0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
0 (0)	0 (0)	1 (5)	0 (0)	2 (10)	0 (0)
0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)
2 (18)	0 (0)	0 (0)	2 (18)	4 (36)	3 (27)
0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
2 (4.4)	0 (0)	0 (0)	0 (0)	4 (8.8)	1 (2.2)
1 (4)	0 (0)	0 (0)	2 (8)	7 (28)	2 (8)
0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
0 (0)	0 (0)	1 (13)	0 (0)	1 (13)	0 (0)
3 (17)	0 (0)	0 (0)	0 (0)	5 (27)	3 (17)
1 (2.1)	0 (0)	0 (0)	1 (2.1)	3 (6.3)	1 (2.1)
1 (2)	0 (0)	0 (0)	1 (2)	4 (9.3)	0 (0)
1 (6)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)
2 (3.2)	0 (0)	2 (3.2)	2 (3.2)	5 (8.1)	3 (4.8)
1 (2.2)	0 (0.0)	1 (2.2)	0 (0)	1 (2.2)	0 (0)
2 (17)	0 (0)	0 (0)	2 (17)	4 (33)	1 (8)
0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)
3 (19)	0 (0)	0 (0)	1 (6)	4 (25)	0 (0)
0 (0)	0 (0)	0 (0)	0 (0)	2 (12)	0 (0)
1 (6)	0 (0)	0 (0)	2 (12)	3 (18)	1 (6)
2 (1.9)	0 (0)	0 (0)	1 (0.9)	5 (4.7)	4 (3.8)
1 (4)	0 (0)	2 (8)	0 (0)	3 (13)	1 (4)
0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
2 (6)	0 (0)	1 (3)	1 (3)	3 (9)	1 (3)
1 (5)	0 (0)	0 (0)	0 (0)	3 (14)	1 (5)
1 (3)	0 (0)	5 (16)	1 (3)	2 (6)	1 (3)
1 (6)	0 (0)	2 (11)	0 (0)	2 (11)	0 (0)
4 (9)	0 (0)	1 (2)	0 (0)	7 (15)	1 (2)
0 (0)	0 (0)	1 (3.5)	0 (0)	2 (6.7)	0 (0)
2 (1.7)	0 (0)	25 (20.8)	1 (0.8)	7 (5.8)	4 (3.3)
0 (0)	2 (9.5)	0 (0)	0 (0)	4 (19.5)	0 (0)
4 (4)	N/A	N/A	1 (1)	N/A	N/A
3 (3.9)	0 (0)	6 (7.7)	2 (2.6)	5 (6.4)	4 (5.1)
5 (2.3)	0 (0)	0 (0)	0 (0)	10 (4.7)	2 (0.9)
1 (2.3)	5 (11.1)	0 (0)	0 (0)	2 (4.5)	1 (2.3)
1 (3)	N/A	0 (0)	1 (3)	4 (12.5)	3 (9)
2 (4.5)	N/A	1 (2)	1 (2)	12 (27.3)	2 (4.5)

Acute arterial occlusion is typically caused by mechanical dissection of the instrumented vessel, thrombus forma-

tion, or severe vasospasm. The occlusion can occur at the site of the target lesion, proximal, or distal to it. Unas-

signed treatment as defined depends of the type of acute occlusion. Acute occlusion does not connote "no re-

flow" caused by microvascular flow limitation, in which the index vessel is patent but has reduced flow. It also does not connote transient closure with reduced flow in which the index treatment application (ie, angioplasty or stent-assisted angioplasty) reverses the closure. Management of acute intraprocedural occlusions includes intra-arterial infusion of a thrombolytic or glycoprotein IIb/IIIa antagonists (54,60). Acute occlusion is not rare during endovascular revascularization (Table 2) but may remain without clinical consequence if rapid revascularization is achieved. All acute occlusions and the unassigned treatment used for recanalization should be presented, including the final clinical outcome. We suggest the use of the following terms: (1) acute occlusion without ischemic stroke: an acute occlusion did not lead to a detectable ischemic stroke after the procedure by clinical examination and neuroimaging; (2) acute occlusion with ischemic stroke, asymptomatic: an acute occlusion leads to a detectable ischemic stroke after the procedure by neuroimaging (CT/MRI) but the neurological examination after the procedure remains unchanged; (3) acute occlusion with ischemic stroke, symptomatic: an acute occlusion occurs during the procedure and leads to a clinically detectable stroke syndrome that is confirmed by adequate neuroimaging (CT or MRI). The stroke may occur even with successful recanalization as determined by angiography. Stroke severity should be reported as an increase from the preprocedure neurological deficit. For example, an increase by ≤ 4 points on the NIHSS compared with baseline is classified as minor procedure-related stroke, and an increase by > 4 points on the NIHSS is classified as major procedure-related stroke. In addition, using the mRS after a period of time, typically 90 days postprocedure, the severity of periprocedural stroke should be classified as nondisabling (mRS ≤ 2) or disabling (mRS > 2).

Subacute Arterial Occlusion

An arterial occlusion occurring after the index procedure is completed and the arterial access to the patient's vasculature has been removed is labeled subacute arterial occlusion. This occlu-

sion can occur up to 4 weeks after the index procedure.

Vessel Dissection

Dissection is defined angiographically by irregular stenosis, "rat tail" stenosis, double lumen, or intimal flaps that may be associated with arterial occlusion. Dissections may be asymptomatic or symptomatic, and this should be mentioned in the results of treated patients. It is graded according to the National Heart Lung and Blood Institute criteria (156): Type A, luminal haziness; Type B, linear dissection; Type C, extraluminal dissection, ie, "cap dissection"; Type D, spiral dissection; Type E, dissection with reduced flow; and Type F, dissection with total occlusion.

Vessel Perforation

Vessel perforation is diagnosed by documentation of contrast material outside the arterial lumen that is either localized in the tissue immediately surrounding the artery or nonfocally beyond the tissue immediately surrounding the artery. Typically, localized extravasation appears as a hematoma, whereas a nonlocalized extravasation leads to a subarachnoid hemorrhage. Arterial perforation may be asymptomatic (detected only on neuroimaging without headache or new neurological signs or symptoms) or symptomatic (associated with headache and/or new neurological symptoms) (70). Treatment of arterial perforations focuses on the type of hemorrhage, intracerebral or subarachnoid, after current treatment recommendations for these 2 hemorrhage types (157,158).

Restenosis

Restenosis after angioplasty and stent-assisted angioplasty is frequent in published case series and catheter-based angiography is the best method to accurately establish the grade of restenosis during the follow-up period. Restenosis can be either asymptomatic or symptomatic. In the prospective intracranial stenting trials, restenosis rates range between 7.5% (159) and 32.4% (2). There is no general agreement about the interval to re-examination to determine if restenosis occurs. Subacute-to-late restenosis is related to intimal hyperplasia (fibromyointimal proliferation)

and vascular remodeling. MRI with MR angiography is useful for noninvasive surveillance, but not all stenoses are detected with these modalities, and measurements of stenosis severity can be inaccurate. The accuracy of CT angiography to depict restenosis is uncertain but often limited by beam-hardening artifact. The lower metal density of the WingSpan stent results in minimal artifact. Some authors advocate rigorous angiographic follow-up beginning 3 months postprocedure given the 33% and 100% incidence of restenosis for Mori Type B and Type C lesions, respectively, at 1 year. In the SSYLVA trial, symptomatic restenosis was common, occurring in 35% of patients. For the WingSpan trial, the rate of restenosis $> 50\%$ was 7.5% at 6 months (53). Therefore, it is recommended that catheter-based angiographic follow-up be performed initially at 3 months, at which stage additional endovascular treatment can be undertaken if required. Depending on patient age, medical condition, and other angiographic risk factors, the value of aggressive arteriographic surveillance must be weighed against the potential complications. In the future, dedicated cerebrovascular stents may receive antiproliferative coatings like coronary stents to prevent restenosis.

Most endovascular surgeons perform repeat angiography 4 to 6 months after the primary intervention or if the patient develops new symptoms.

Recommendations

Anatomic outcome reporting should include definitions and rates of technical success, acute and subacute arterial occlusions with or without subsequent ischemic stroke, vessel dissection, and vessel perforation and should include angiographic measurement of residual stenosis at all follow-up time points. The timing of each of these anatomic outcome events in relation to the procedure should be reported. Assessment of restenosis should be performed by catheter-based angiography as clinically indicated, but should be performed at 6 and 12 months after the endovascular

revascularization and in yearly intervals thereafter.

Clinical outcomes.—The most critical outcome measures are death from any cause, vascular death, myocardial infarction, brain hemorrhage, and ischemic strokes. Events occurring within 30 days of the procedure are typically referred as procedure-related complications.

The landmark study, WASID, defined vascular death other than stroke as either sudden death or death within 30 days after myocardial infarction, pulmonary embolism, rupture of an aortic aneurysm, acute ischemia of a limb or internal organ, subdural or subarachnoid hemorrhage, or major systemic hemorrhage (49). Like in other stroke trials, ischemic stroke was defined as a new focal neurological deficit lasting for at least 24 hours not associated with a brain hemorrhage on neuroimaging and a transient ischemic attack as a new focal neurological deficit lasting <24 hours. A brain hemorrhage was defined as evidence of blood in the brain on neuroimaging.

The definition of transient ischemic attacks has undergone recent revision. Based on modern neuroimaging and clinical outcome data, patients with symptoms lasting up to 24 hours associated with diffusion-weighted imaging-positive lesions on MRI are now classified as ischemic strokes and not as transient ischemic attacks (160). This classification is widely accepted and should be used for outcome reporting after intracranial revascularization.

Ischemic and hemorrhagic strokes are typically classified as either disabling (major) or nondisabling (minor). There is no unique definition for a disabling stroke. WASID defined a disabling stroke as a mRS ≥ 3 within 30 days after stroke (49), a definition that is widely used in acute stroke trials. In contrast, SSYLVA and the WingSpan trials used an NIHSS ≥ 15 , mRS ≥ 4 , or a Barthel Index ≤ 60 points for the definition of a disabling stroke (2,53). Whatever definition is used, ipsilateral and contralateral stroke rates are important, require definition of criteria for diagnosis, and finally must be carefully reported.

Endovascular recanalization may lead to stroke by 3 different mechanisms: (1) occlusion of the target vessel; (2) distal embolization in the territory of the target vessel; and (3) side

branch occlusion. Each of these pathological mechanisms requires different therapeutic approaches. The presumed pathological mechanism of periprocedural acute ischemic strokes based on this classification should be presented.

Patients undergoing endovascular procedures are placed on antithrombotic treatment (eg, heparin, platelet inhibitors) that may predispose to hemorrhagic complications. Major hemorrhage is typically defined as any symptomatic intracranial hemorrhage or systemic hemorrhage requiring hospitalization, blood transfusion, or surgery. There is no unique definition of a symptomatic intracerebral hemorrhage. Acute thrombolysis trials use this term to describe a documented intracerebral hemorrhage by neuroimaging that is associated with a deterioration of the patient's neurological condition. The National Institutes of Neurological Disorders and Stroke Study defined any deterioration associated with an intracerebral hemorrhage as symptomatic, irrespective of the severity as assessed by the NIHSS (161). In the European Cooperative Acute Stroke Studies (1 and 2), an intracerebral hemorrhage had to be associated with an increase of the NIHSS ≥ 4 points to qualify as symptomatic (162–164). The European Cooperative Acute Stroke Studies definition has been shown to be associated with large hematoma size causing significant disability and may for that reason be clinically more robust compared with the National Institute of Neurological Disorders and Stroke definition of symptomatic intracerebral hemorrhage.

Patients with intracranial atherosclerosis often have associated coronary artery disease. Major cardiac events are important outcome measures and were defined as either myocardial infarction or sudden death in WASID.

Clinical events as defined here translated into functional disability and discharge destination is another measure of outcome after an endovascular intervention. Typical discharge destinations are home without support services, home with support services, nursing home, acute or subacute rehabilitation facility, and death.

The time from endovascular intervention to occurrence of one of the previously defined outcome events is

Table 3
Definitions of Complications

Minor complications
No therapy, no consequence
Nominal therapy, no consequence; includes overnight admission for observation only
Major complications
Require therapy, minor change in length of hospitalization (<48 hours)
Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 hours)
Permanent adverse sequelae
Death

important and if the length of the follow-up period allows, mean annual rates for each of these events using appropriate statistical calculations should be reported. Event rates are reported at various times after the procedure. Typical periods are at discharge, 30 days, 90 days, 6 months, and 1 year after the intervention. The choice of time interval in reporting outcome events is critical because this may affect the overall study result. For example, if a patient sustains an ischemic stroke at Day 15 after the procedure, then his or her Day 30-assessed disability using the mRS may be 4. However, many patients will experience some recovery after a stroke; because of a partial recovery over the subsequent few weeks, the patient may have a mRS of 3 at 90 days post-procedure. For this reason, changes in the mRS over time may be a more meaningful way to present study results, a method that was recently used in the NXY-059 acute ischemic stroke trial (14). In any event, methods must be consistent and disclosed.

A special consideration is the occurrence of hyperperfusion syndrome after intracranial revascularization (108, 131,165,166). This is a known complication of both carotid endarterectomy (104) and carotid stenting (108,167–169). Hyperperfusion syndrome is characterized by acute development of focal neurological symptoms that may be associated with simple or complex-focal seizures attributable to the vascular territory distal to the revascularized artery within a few days after the procedure. This complication may develop either secondary to cerebral

Table 4
Classification of Complications by Systems

Complication	Class
Abscess	Infectious/inflammatory
Acute coronary syndrome (ST or non-ST elevation infarction)	Cardiac
Angina	Cardiac
Idiosyncratic reaction	Medication-related
Allergic/anaphylactoid reaction	Contrast-related
Arrhythmia	Cardiac
Arterial occlusion/thrombosis, puncture site	Vascular
Arterial occlusion/thrombosis, remote from puncture site	Vascular
Arteriovenous fistula	Vascular
Coagulopathy	General nonvascular
Congestive heart failure	Cardiac
Device malfunction with adverse effect	Device-related
Death, related to procedure (30-day mortality)	Death
Death, unrelated to procedure (30-day mortality)	Death
Embolization, arterial (air, tissue, or thrombotic tissue)	Vascular
Fever	Infectious/inflammatory
Fluid/electrolyte imbalance	General nonvascular
Hematoma bleed, remote site	Vascular
Hematoma bleed at needle, device path: nonvascular procedure	Vascular
Hematoma bleed, puncture site: vascular procedure	Vascular
Incorrect drug	Medication-related
Incorrect dosage	Medication-related
Ischemia/infarction of tissue/organ	Vascular
Incorrect site of administration	Medication-related
Hypoxia	Respiratory/pulmonary
Local infection	Infectious/inflammatory
Liver failure	General nonvascular
Myocardial infarction (ST or non-ST elevation infarction)	Cardiac
Malposition	Device-related
Nausea/vomiting	General nonvascular
Pancreatitis	Infectious/inflammatory
Pulmonary embolism	Respiratory/pulmonary
Peritonitis	Infectious/inflammatory
Pulmonary edema	Respiratory/pulmonary
Peripheral nervous system complication	Neurologic
Pneumothorax	Respiratory/pulmonary
Pseudoaneurysm	Vascular
Respiratory failure	Respiratory/pulmonary
Renal failure (transient or persistent)	Contrast-related
Septicemia/bacteremia	Infectious/inflammatory
Seizure	Neurologic
Septic shock	Infectious/inflammatory
Stent migration	Device-related
Stent misplacement	Device-related
Stent occlusion	Device-related
Stent embolization	Device-related
Stent thrombosis	Device-related
Stroke, ischemic (major or minor)	Neurologic
Stroke, hemorrhagic (major or minor)	Neurologic
Tissue extravasation	Contrast-related
Transient ischemic attack	Neurologic
Unintended perforation of hollow viscus	General nonvascular
Vascular perforation or rupture	Vascular
Vagal reaction	Cardiac
Vasospasm	Vascular
Venous occlusion/thrombosis, puncture site	Vascular
Venous occlusion/thrombosis, remote from puncture site	Vascular
Vessel perforation	Vascular
Vessel rupture	Vascular
Vessel thrombosis	Vascular
Vessel trauma requiring surgical repair or intervention	Vascular

Table 5
Recommendations for Reporting Standards

	Required	Highly Recommended	Recommended
Preprocedural data			
Patient population (see Table 1)	X		
Neurological history	X		
Primary symptom necessitating treatment	X		
Presumed pathophysiology of symptoms leading to intervention	X		
Risk factors	X		
Comorbidities	X		
Study design			
Inclusion criteria	X		
Exclusion criteria	X		
Primary point(s)	X		
Secondary point(s)		X	
Degree of stenosis	X		
Lesion location	X		
Lesion no.	X		
Prior medical therapy (see Table 1)	X		
Procedure data			
Level of experience		X	
Description of revascularization procedure	X		
Preprocedure stenosis grade and length	X		
Postprocedure stenosis grade and length	X		
Pharmacologic adjuncts	X		
Complications	X		
Hospital days	X		
Intensive care unit days	X		
Postprocedural data			
Stratification by symptoms, high-risk categories	X		
Stroke			
Reversible versus permanent	X		
Major versus minor	X		
Ipsilateral versus total	X		
Ischemic versus hemorrhagic at 30 days, 6 months, and 12 months	X		
Annualized rate of stroke	X		
"Subsequent" annualized rate of stroke			X
Myocardial infarction at 30 days	X		
Mortality at days, 6 months, and 12 months	X		
Recurrent stenosis at 12 months	X		
Target lesion revascularization	X		

edema formation or intracerebral hemorrhage in the successfully reperfused cerebral tissue. Hyperperfusion syndrome is thought to result from dysautoregulation from rapidly increased blood flow in a previously metabolically deprived vascular territory well beyond the metabolic demands of the brain tissue affected, thus leading to perfusion breakthrough in the cerebral capillaries. Prevention of this potentially fatal complication is usually performed by excluding patients with recent ischemic strokes, very tight blood pressure management after revascularization, and strict control of intra- and immediate postprocedure anticoagulation with intravenous heparin keeping the

partial thromboplastin time at no more than 2.5 times of the normal value (108,165,166).

Recommendations

A detailed description of type and timing of clinical events occurring during the procedure and the follow-up period should be reported. The clinical event reporting should include rates of ischemic and hemorrhagic strokes stratified in ipsilateral and contralateral sides in relation to the treated vessel, stroke severity using a validated scale (for example, NIHSS), disability using validated scales (for example Barthel Index or mRS) at defined follow-up points

postintervention, and death from cardiovascular or other causes. After the updated definition of transient ischemic attack, an ischemic event associated with an appropriate diffusion-weighted imaging abnormality should be considered a stroke even if the symptoms resolve within 24 hours. Events occurring within 30 days after endovascular revascularization should be considered periprocedural. All patients should be examined by a stroke neurologist after the procedure.

Complications of intracranial endovascular revascularization.—Angiographic and clinical events occurring during the procedure or the follow-up period may be immediate or delayed complications of the endovascular procedure.

Reporting of complications is crucial. Complications can be defined as minor or major and both should be reported. Minor complications are those that do not require a specific or a nominal therapy and have no consequence. Complications that require overnight admission for observation only are classified as minor. Major complications require hospitalization for a specific therapy beyond pure observation and may be associated with an increased level of care, permanent adverse sequelae, and death (**Table 3**). **Table 4** lists typical complications associated with endovascular procedures. Differentiation of complications related or not related to the endovascular procedure should be attempted. **Table 2** shows complication rates reported in the literature for intracranial endovascular revascularization procedures. Complications occurring within 30 days after endovascular revascularization are considered perioperative and procedure-related. Classification and terminology of complications follows the definitions as described in detail in the "Anatomic Outcome" and "Clinical Outcome" sections.

CONCLUSION

Endovascular revascularization for intracranial atherosclerosis is an emerging new treatment option for symptomatic patients. Symptomatic patients are defined as those with transient ischemic attacks or ischemic strokes in the territory of the stenotic artery. As technology is emerging, the number of patients treated is increasing and will continue to increase. Standardized reporting of the clinical experience across different institutions assures comparability of results to define the benefits and risks of this intervention across different patient populations. **Table 5** summarizes recommendations for result reporting.

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