AMERICAN ACADEMY OF NEUROLOGY

Special Article

CME

Assessment: Transcranial Doppler ultrasonography

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology*

M.A. Sloan, MD, MS; A.V. Alexandrov, MD, RVT; C.H. Tegeler, MD; M.P. Spencer, MD; L.R. Caplan, MD; E. Feldmann, MD; L.R. Wechsler, MD; D.W. Newell, MD; C.R. Gomez, MD; V.L. Babikian, MD; D. Lefkowitz, MD; R.S. Goldman, MD; C. Armon, MD, MHS; C.Y. Hsu, MD, PhD; and D.S. Goodin, MD

Abstract—*Objective:* To review the use of transcranial Doppler ultrasonography (TCD) and transcranial color-coded sonography (TCCS) for diagnosis. *Methods:* The authors searched the literature for evidence of 1) if TCD provides useful information in specific clinical settings; 2) if using this information improves clinical decision making, as reflected by improved patient outcomes; and 3) if TCD is preferable to other diagnostic tests in these clinical situations. *Results:* TCD is of established value in the screening of children aged 2 to 16 years with sickle cell disease for stroke risk (Type A, Class I) and the detection and monitoring of angiographic vasospasm after spontaneous subarachnoid hemorrhage (Type A, Class I to II). TCD and TCCS provide important information and may have value for detection of intracranial stenoocclusive disease (Type B, Class II to III), vasomotor reactivity testing (Type B, Class II to III), detection of cerebral circulatory arrest/brain death (Type A, Class II), monitoring carotid endarterectomy (Type B, Class II to III), monitoring cerebral thrombolysis (Type B, Class II to III), and monitoring coronary artery bypass graft operations (Type B to C, Class II to III). Contrast-enhanced TCD/TCCS can also provide useful information in right-to-left cardiac/extracardiac shunts (Type A, Class II), intracranial occlusive disease (Type B, Class II to IV), and hemorrhagic cerebrovascular disease (Type B, Class II to IV), although other techniques may be preferable in these settings.

NEUROLOGY 2004;62:1468–1481

Transcranial Doppler (TCD) is a noninvasive ultrasonic technique that measures local blood flow velocity and direction in the proximal portions of large intracranial arteries.[1] TCD is operator dependent and requires training and experience to perform and interpret results. TCD is performed by technologists, sonographers, and physicians and is interpreted by neurologists and other specialists.

TCD is used principally in the evaluation and management of patients with cerebrovascular disease. Conventional and digital subtraction angiography (DSA), where available, constitute the "reference standard" for evaluating patency and degree of stenosis in intracranial vessels.

The chief advantages of TCD are as follows: It can be performed at the bedside and repeated as needed or applied for continuous monitoring; it is frequently less expensive than other techniques; and dye contrast agents are not used. Its chief limitation is that it can demonstrate cerebral blood flow velocities only in certain segments of large intracranial vessels, although large-vessel intracranial arterial disease commonly occurs at these locations. In general, TCD is most useful when the clinical question pertains to

*See Appendix 1 on page 1479 for a complete list of Subcommittee members.

From Rush University Medical Center (Dr. Sloan), Chicago, IL; University of Texas Houston Medical Center (Dr. Alexandrov); School of Medicine, Wake Forest University (Drs. Tegeler and Lefkowitz), Winston-Salem, NC; Institute of Applied Physiology and Medicine (Dr. Spencer), Seattle, WA; Beth Israel Deaconess Medical Center (Dr. Caplan), Boston, MA; School of Medicine, Brown University (Dr. Feldmann), Providence, RI; University of Pittsburgh Medical Center (Dr. Wechsler), PA; University of Washington (Dr. Newell), Seattle; Alabama Neurological Institute (Dr. Gomez), Birmingham; Boston University School of Medicine (Dr. Babikian), MA; Aurora Medical Group (Dr. Goldman), Milwaukee, WI; Baystate Medical Center (Dr. Armon), Springfield, MA; Washington University School of Medicine (Dr. Hsu), St. Louis, MO; and University of California at San Francisco (Dr. Goodin).

Approved by the Therapeutics and Technology Assessment Subcommittee on August 8, 2003. Approved by the Practice Committee on November 8, 2003. Approved by the Board of Directors on January 18, 2004.

Received August 28, 2003. Accepted in final form March 1, 2004.

Address correspondence and reprint requests to American Academy of Neurology, 1080 Montreal Ave, St. Paul, MN 55116.

Table 1 *Definitions for classification of evidence*

Rating of recommendations	Translation of evidence to recommendation	Rating of diagnostic article	Rating of prognostic article
A = established as useful/predictive or not useful/predictive for the given condition in the specified population.	≥1 convincing Class I or ≥2 consistent, convincing Class II studies.	Class I: evidence provided by prospective study in broad spectrum of persons with suspected condition, using a "gold standard" to define cases, where test is applied in blinded evaluation, and enabling assessment of appropriate tests of diagnostic accuracy.	Class I: evidence provided by prospective study in broad spectrum of persons who may be at risk of outcome (target disease, work status). Study measures predictive ability using independent gold standard to define cases. Predictor is measured in evaluation masked to clinical presentation. Outcome is measured in evaluation masked to presence of predictor.
B = probably useful/predictive or not useful/predictive for the given condition in the specified populations.	≥1 convincing Class II or ≥3 consistent Class III studies.	Class II: evidence provided by prospective study in narrow spectrum of persons with suspected condition or well-designed retrospective study of broad spectrum of persons with suspected condition (by "gold standard") compared with broad spectrum of controls where test is applied in blinded evaluation and enabling assessment of appropriate tests of diagnostic accuracy.	Class II: evidence provided by prospective study of narrow spectrum of persons who may be at risk for having the condition, retrospective study of broad spectrum of persons with condition compared with broad spectrum of controls. Study measures prognostic accuracy of risk factor using acceptable independent gold standard to define cases. Risk factor is measured in evaluation masked to the outcome.
C = possibly useful/predictive or not useful/predictive for the given condition in the specified population.	≥2 convincing and consistent Class III studies.	Class III: evidence provided by retrospective study where either persons with established condition or controls are of narrow spectrum and where test is applied in blinded evaluation.	Class III: evidence provided by retrospective study where persons with condition or controls are of narrow spectrum. Study measures predictive ability using independent gold standard to define cases. Risk factor measured in evaluation masked to outcome.
D = data inadequate or conflicting. Given current knowledge, test/predictor unproven.	—	Class IV: any design where test is not applied in blinded fashion *or* evidence provided by expert opinion or descriptive case series.	Class IV: any design where predictor is not applied in masked evaluation *or* evidence by expert opinion, case series.

those vessel segments. However, in some settings, TCD can detect indirect effects such as abnormal waveform characteristics suggestive of proximal hemodynamic or distal obstructive lesions. This limitation also applies to MR angiography (MRA) and CT angiography (CTA). Even DSA and conventional angiography may be inconclusive if all relevant vessels are not fully imaged. The reference standard vs TCD must be appropriate to the clinical setting.

Methods. We reviewed summary statements[1,2] and other articles, based on selection of relevant publications cited in these new articles and additional Medline search through June 2003, using the American Academy of Neurology rating system (table 1).[3] When data were inconclusive, a U rating was given. Articles reviewed and cited herein reflect a mixture of diagnostic, therapeutic, or prognostic information used as the reference standard in individual studies. Sensitivity and specificity reflect the ability of a diagnostic test to detect disease. For the purposes of this review, ratings of sensitivity and specificity were operationally defined as excellent (≥90%), good (80 to 89%), fair (60 to 79%), and poor (<60%). We review the sensitivity and specificity of TCD (table 2) and transcranial color-coded sonography (TCCS) (table 3) for various disease states.

The clinical utility of a diagnostic test may be operationally defined as the value of the test result to the clinician caring for the individual patient. In this sense, value to the clinician refers to the ability of a diagnostic test to detect the disease process of interest, influence patient care, or provide prognostic information when compared with an appropriate reference standard or in a well-designed clinical trial. We summarize the clinical utility (table 4) of TCD/TCCS and focus on the clinical indications for which conclusions can be drawn.

Results. *Conventional or nonimaging TCD.* Ischemic cerebrovascular disease. *Sickle cell disease.* In children with sickle cell disease, ischemic cerebral

Table 2 *Accuracy of TCD ultrasonography by indication*

Indication	Sensitivity, %	Specificity, %	Reference standard	Evidence/ Class
Sickle cell disease	86	91	Conventional angiography	A/I
Right-to-left cardiac shunts	70–100	>95	Transesophageal echocardiography	A/II
Intracranial steno-occlusive disease			Conventional angiography	
Anterior circulation	70–90	90–95		B/II–III
Posterior circulation	50–80	80–96		B/III
Occlusion				
MCA	85–95	90–98		B/III
ICA, VA, BA	55–81	96		B/III
Extracranial ICA stenosis			Conventional angiography	
Single TCD variable	3–78	60–100		C/II–III
TCD battery	49–95	42–100		C/II–III
TCD battery and carotid duplex	89	100		C/II–III
Vasomotor reactivity testing				
≥70% extracranial ICA stenosis/occlusion			Conventional angiography, clinical outcomes	B/II–III
Carotid endarterectomy			EEG, MRI, clinical outcomes	B/II
Cerebral microembolization			Experimental model, pathology, MRI, neuropsychological tests	
General				B/II–IV
Coronary artery bypass graft surgery microembolization				B/II–III
Prosthetic heart valves				C/III
Cerebral thrombolysis			Conventional angiography, MR angiography, clinical outcome	B/II–III
Complete occlusion	50	100		
Partial occlusion	100	76		
Recanalization	91	93		
Vasospasm after spontaneous subarachnoid hemorrhage:			Conventional angiography	I –II
Intracranial ICA	25–30	83–91		
MCA	39–94	70–100		
ACA	13–71	65–100		
VA	44–100	82–88		
BA	77–100	42–79		
PCA	48–60	78–87		
Vasospasm after traumatic subarachnoid hemorrhage			Conventional angiography	I –III
Cerebral circulatory arrest and brain death	91–100	97–100	Conventional angiography, EEG, clinical outcome	II

TCD = transcranial Doppler; MCA = middle cerebral artery; ICA = internal carotid artery; VA = vertebral artery; BA = basilar artery; ACA = anterior cerebral artery; PCA = posterior cerebral artery.

infarction is associated with an occlusive vasculopathy involving the distal intracranial internal carotid artery (ICA) and the proximal portions of the middle (MCA) and anterior (ACA) cerebral arteries. One large cohort study with long-term follow-up showed that elevated time-averaged mean maximum blood flow velocity of ≥200 cm/s in the ICA or MCA by TCD is strongly associated with stroke risk.[4] With use of this flow velocity criterion, the Stroke Prevention Trial in Sickle Cell Anemia showed that periodic blood transfusion therapy to lower the hemoglobin S concentration to <30% of total hemoglobin concentration in children between the ages of 2 and 16 years resulted in a 92% reduction in stroke risk.[5]

TCD screening of children with sickle cell disease between the ages of 2 and 16 years is effective for assessing stroke risk (Type A, Class I evidence), although the optimal frequency of testing is unknown (Type U).

Right-to-left cardiac shunts. Paradoxical embolism via a patent foramen ovale (PFO) is a cause of stroke in young adults.[6-9] The presence of an atrial septal aneurysm may increase the stroke risk of a PFO with right-to-left shunting.[8,9] Data show a high

Table 3 *Accuracy of TCCS by indication*

Indication	Sensitivity, %	Specificity, %	Reference standard	Evidence/ Class
TCCS, with/without contrast enhancement			Conventional angiography, pathology	II–IV
ACoA collateral flow	100	100		
PCoA collateral flow	85	98		
Intracranial steno-occlusive lesions				
Any	Up to 100	Up to 83		
≥50% stenosis				
MCA	100	100		
ACA	100	100		
VA	100	100		
BA	100	100		
PCA	100	100		
Parenchymal hypoechogenicity in MCA distribution	69	83	CT scan	III
Vasospasm after spontaneous subarachnoid hemorrhage:			Conventional angiography	II–IV
Intracranial ICA	100	97		
MCA	100	93		
ACA	71	85		
Intracerebral hemorrhage	94	95	CT scan	

TCCS = transcranial color-coded sonography; ACoA = anterior communicating artery; PCoA = posterior communicating artery; MCA = middle cerebral artery; ACA = anterior cerebral artery; VA = vertebral artery; BA = basilar artery; PCA = posterior cerebral artery; ICA = internal carotid artery.

correlation between contrast-enhanced TCD and contrast-enhanced transesophageal echocardiography (TEE), with essentially 100% concordance for the "clinically significant" high number of particles shunted. Nevertheless, the sensitivity and specificity of contrast TCD for detecting right-to-left cardiac or extracardiac (pulmonary arteriovenous) shunts may vary by center, protocol, and diagnostic criteria.[10-12] The routine performance of the Valsalva maneuver during testing can improve sensitivity and specificity. The sensitivity of contrast TCD can also be improved by using a higher volume of agitated saline (10 mL instead of 5 mL), use of Echovist (especially Echovist-300) instead of agitated saline, or repeating the Valsalva maneuver if the initial result is negative.[12]

Contrast TCD is comparable with contrast TEE for detecting right-to-left shunts due to PFO (Type A, Class II evidence). However, TEE is better than contrast TCD because it provides direct anatomic information regarding the site and nature of the shunt or presence of an atrial septal aneurysm. Whereas the number of microbubbles reaching the brain can be quantified by TCD, the therapeutic impact of this additional information is unknown (Type U).

Table 4 *Definitions for clinical utility*

1. Able to provide information and clinical utility established.
2. Able to provide information and clinical utility, compared with other diagnostic tools, remains to be determined.
3. Able to provide information, but clinical utility remains to be determined.
4. Able to provide information, but other diagnostic tests are preferable in most cases.

Intracranial steno-occlusive disease. Intracranial atherosclerosis is responsible for up to 10% of TIA and strokes.[13,14] Stenosis and occlusion of the ICA siphon, proximal (M1) segment of the MCA, intracranial vertebral artery (VA), proximal basilar artery (BA), and proximal (P1) segment of the posterior cerebral artery (PCA) can be reliably detected by TCD.[1,15-31] The relative performance of TCD vs MRA, conventional angiography, or DSA varies by center, characteristics and prevalence of disease in the study population, diagnostic criteria, and technical expertise. Sensitivity, specificity, positive predictive value, and negative predictive value of TCD are generally higher in the anterior circulation than in the vertebrobasilar circulation owing to more variable anatomy and technical difficulties in insonation of the vertebrobasilar circulation.

Data are beginning to define TCD criteria for >50% stenosis of large intracranial arteries.[15,26] Intracranial arterial stenotic lesions in the internal carotid distribution are dynamic and can evolve over time, with increasing or decreasing flow velocities and appearance of new collateral patterns, the latter

suggesting further hemodynamic compromise distal to the stenotic lesion.[27-29] In two recent studies in small, highly selected populations[28,29] using peak systolic[29] or mean flow[28] velocities and variable noninvasive criteria for change in degree of stenosis, progression of MCA stenosis was associated with new ipsilateral stroke or TIA[28] or major vascular events.[28,29] Data are insufficient to establish TCD criteria for >50% stenosis or for progression of stenosis in intracranial arteries (Type U).

Acute cerebral infarction. Cerebral angiography shows acute occlusion in 76% of acute MCA territory infarcts within 6 hours of stroke onset.[30] TCD can detect these angiographic occlusions with high (>90%) sensitivity, specificity, positive predictive value, and negative predictive value.[20,21,26,30] In addition, TCD can detect ICA siphon, VA, and BA occlusions with fair to good (70 to 90%) sensitivity and positive predictive value and excellent specificity and negative predictive value occlusions.[31]

Intracranial arterial occlusions detected by TCD are associated with poor neurologic recovery, disability, or death after 90 days,[22,23] whereas normal results predict early improvement.[25,32] In patients with acute ICA territory stroke, TCD findings, stroke severity at 24 hours, and CT lesion size were independent predictors of outcome after 30 days.[22] When combined with carotid duplex sonography, the presence and total number of arteries with suspected steno-occlusive lesions (especially intracranial) by TCD in patients with TIA or ischemic stroke were associated with an increased risk of further vascular events (usually stroke) and death within 6 months.[24] TCD-detected M1 MCA occlusions within 6 hours of stroke onset may be an independent predictor of spontaneous hemorrhagic transformation, with a positive predictive value of 72%.[33] A recent study[34] showed that delayed (>6-hour) spontaneous recanalization was independently associated (odds ratio [OR] = 8.9, 95% CI = 2.1 to 33.3) with hemorrhagic transformation.

TCD is probably useful for the evaluation of patients with suspected intracranial steno-occlusive disease, particularly in the ICA siphon and MCA (Type B, Class II to III evidence). The relative value of TCD compared with MRA or CTA remains to be determined (Type U). Data are insufficient to give a recommendation regarding replacing conventional angiography with TCD (Type U).

Extracranial ICA stenosis. TCD can detect the hemodynamic consequences of severe extracranial ICA stenosis, such as reversal of the direction of ophthalmic artery flow, presence of collateral flow patterns, absence of ophthalmic or carotid siphon flow, and reduced MCA flow velocity and pulsatility.[34,35] For patients with angiographically or pathologically confirmed stenosis of >70%, accuracy varies according to diagnostic criteria. Use of single TCD measurements or a battery of TCD measurements has variable sensitivity and specificity. However, when highly specific carotid duplex criteria are added, sensitivity and specificity are considerably improved.[35-37]

TCD is possibly useful for the evaluation of severe extracranial ICA stenosis or occlusion (Type C, Class II to III evidence).

Vasomotor reactivity testing. TCD evaluation of large basal conducting vessels, which remain relatively constant in diameter during moderate pressure fluctuations or changes in microcirculatory function, can provide an index of relative flow changes in response to small blood pressure changes and physiologic stimuli to assess autoregulation and vasomotor reactivity (VMR) of the distal cerebral arteriolar bed. VMR testing techniques of static (i.e., at rest) or dynamic (i.e., after provocative stimuli) cerebral autoregulation include measuring changes in flow velocities following 1) hemodynamic stimuli (rapid leg cuff deflation, Valsalva maneuver, deep breathing, ergometric exercise, head-down tilting, orthostasis and lower body negative pressure, beat-to-beat spontaneous transient pressor and depressor changes in mean arterial pressure), 2) CO_2 inhalation (hypercapnia/hyperventilation hypocapnia), 3) the breath-holding index (BHI), 4) acetazolamide injection, and 5) the transient hyperemia response and its variants.[38-46]

VMR testing techniques with TCD have been used to evaluate patients with symptomatic or asymptomatic extracranial ICA stenosis or occlusion,[38-45] cerebral small-artery disease, head injury, and aneurysmal subarachnoid hemorrhage (SAH).[46] Although TCD may detect abnormalities of cerebral hemodynamics (increased or decreased pulsatility) in patients with risk factors for or symptoms of cerebrovascular disease,[39] the value of TCD evaluation of cerebral hemodynamic impairment and stroke risk has recently been questioned.[47]

In a recent study[43] of patients with asymptomatic 70% extracranial ICA stenosis, the annual ipsilateral ischemic event rate was 4.1% with normal BHI and 13.9% with impaired BHI. In patients with severe (>70%) symptomatic ICA extracranial stenosis, VMR in the ipsilateral MCA is significantly reduced.[40] Patients with impaired collateral blood flow patterns may have the greatest reduction in VMR.[41] One recent study[39] showed that exhausted VMR in the ipsilateral MCA was an independent predictor of the occurrence of ipsilateral TIA and stroke (OR = 14.4, 95% CI = 2.63 to 78.74). In patients with asymptomatic extracranial ICA occlusion, a BHI of <0.69 reliably distinguishes pathologically reduced from normal cerebral VMR and identifies patients at risk for stroke and TIA.[42]

TCD vasomotor reactivity testing is considered probably useful for the detection of impaired cerebral hemodynamics in patients with asymptomatic severe (>70%) stenosis of the extracranial ICA, patients with symptomatic or asymptomatic extracranial ICA occlusion, and patients with cerebral small-artery disease (Type B, Class II to III evidence). How the results from these techniques should be used to in-

fluence therapy and affect patient outcomes remains to be determined (Type U).

Detection of cerebral microembolic signals. The physics and technical aspects of ultrasonic detection of microembolic signals or "high-intensity transient signals" ("HITS") by TCD have recently been reviewed.[1,48,49] Particulate (solid, fat) and gaseous materials in flowing blood have different acoustic impedance properties than surrounding red blood cells. The Doppler ultrasound beam is both reflected and scattered at the interface between the embolus and blood, resulting in an increased intensity of the received Doppler signal. The hierarchy of backscatter of the ultrasound, in descending order, is gaseous emboli, solid emboli, and normal-flowing blood (including transient red blood cell aggregates).

Microembolic signals have been detected in patients with asymptomatic and symptomatic high-grade internal carotid stenosis, prosthetic cardiac valves, myocardial infarction, atrial fibrillation, aortic arch atheroma, fat embolization syndrome, and retinal or general cerebral vascular disease. In addition, these signals occur in coronary catheterization, coronary angioplasty, direct current cardioversion, cerebral angiography, carotid endarterectomy (CEA), carotid angioplasty, and cardiopulmonary bypass. TCD can be used to localize the embolic source or monitor the effects of antithrombotic treatment in patients with atherosclerotic cerebrovascular disease.[50] In patients with high-grade carotid stenosis, sources of asymptomatic microembolic signals may include ulcerated plaques[51] and microscopic platelet aggregates and fibrin clots.[52] Asymptomatic cerebral microembolization was associated with an increased risk of further cerebral ischemia (OR = 8.10, 95% CI = 1.58 to 41.57) in this setting.[51]

Comparison between studies is difficult because of differences in diagnostic criteria and detection threshold, different instruments, different instrument settings, nature and severity of disease, variability in occurrence of microembolic signals, time between last symptom and detection of microembolic signals, and type of treatment.[1,49] Interobserver agreement for microembolic signal detection and determination of signal type is variable; a higher detection threshold results in higher specificity and intercenter agreement.[48] New hardware and software technical capabilities may help detection of microembolic signal type and discrimination from artifact. However, accurate and reliable characterization of embolus size and composition is not possible with current technology. In addition, data have not shown that detection of microembolic signals leads to improved patient outcomes.

TCD is probably useful to detect cerebral microembolic signals in a wide variety of cardiovascular/cerebrovascular disorders/procedures (Type B, Class II to IV evidence). However, current data do not support the use of TCD for diagnosis or for monitoring response to antithrombotic therapy in ischemic cerebrovascular disease (Type U).

Perioperative and periprocedural monitoring. *CEA.* The principal cause of stroke following CEA, particularly in the postoperative phase, is embolism from the operative site.[53] TCD monitoring of the ipsilateral MCA during CEA allows real-time readout of velocity changes in the basal cerebral arteries. Although a precise percentage decrease in flow velocity from baseline or a velocity threshold that predisposes to cerebral ischemia has not been established, a large decrease in velocities intraoperatively is considered an indication for pharmacologic blood pressure augmentation, shunt placement, or repair of shunt kinking or thrombosis. In addition, flow velocity changes during cross-clamping correlate with stump pressure measurements.[54] Reports of combined intraoperative TCD monitoring and EEG monitoring show that although there is high overlap between low MCA flow velocities and ipsilateral EEG slowing, neither technique may identify all candidates for shunting or prevent all strokes.[54-56] Hemodynamic changes following CEA include an improvement in MCA, ACA, and ophthalmic flow velocities, resolution of side-to-side MCA flow velocity asymmetries, and restoration of cerebrovascular vasoreactivity to CO_2 or acetazolamide challenge.[40,57,58]

Microembolic signals most commonly occur during the dissection phase intraoperatively, during shunting and unclamping, during wound closure, and in the first few hours postoperatively.[59-66] The number of microembolic signals during dissection correlates best with new ischemic lesions seen on MRI[62] and postoperative cognitive deterioration.[59] The presence of >50 microembolic signals/hour during the early postoperative phase is reported to predict the development of ipsilateral focal cerebral ischemia.[60] TCD-detected microembolic signals during dissection and wound closure, >90% MCA velocity decrease at cross-clamping, and >100% pulsatility index increase at clamp release have been associated with intraoperative stroke.[63] In one study of 500 CEA operations monitored with TCD,[53] the occurrence of stroke decreased from 7% during the first 100 TCD-monitored operations to 2% in the last 400 TCD-monitored operations. In another report, a policy of quality control assessment (TCD monitoring and completion angioscopy) substantially reduced the occurrence of intraoperative stroke.[64] Postoperative TCD monitoring may identify patients at risk for carotid thrombosis[59,60] or ipsilateral hemispheric ischemia who may benefit from Dextran-40 therapy.[61,66] TCD may also be used to noninvasively monitor the effect of novel antiplatelet agents on the frequency of microembolic signals following CEA.[67]

CEA monitoring with TCD can provide important feedback pertaining to hemodynamic and embolic events during and after surgery that may help the surgeon take appropriate measures at all stages of the operation to reduce the risk of perioperative stroke. TCD monitoring is probably useful during and after CEA in circumstances where monitoring is felt to be necessary (Type B, Class II to III evidence).

Coronary artery bypass graft surgery. Postoperative neurologic complications such as cerebral infarc-

tion and encephalopathy occur in up to 15% of patients who undergo coronary artery bypass graft (CABG) surgery; up to 70% of patients have neuropsychological deficits.[68-72] The risk of stroke after CABG can be predicted based on characteristics known before surgery.[70-72]

TCD monitoring can document flow velocity changes in all phases of the operation. There have been no reports of correlations between changes in flow velocities or CO_2 reactivity and neurologic outcome. Cerebral microembolic signals of all types may be detected at all phases of the operation, especially during aortic cannulation, aortic cross-clamping, and clamp removal.[73] There is a significant correlation between the number of emboli detected by TCD and TEE.[73] TCD demonstration of the presence of microembolic signals, with higher number of microembolic signals associated with postoperative neuropsychological abnormalities, led to the acceptance of membrane over bubble oxygenators during cardiopulmonary bypass.[74] Recent data suggest that distal aortic arch cannulation[75] or off-pump technique[76,77] may be associated with lower numbers of cerebral microemboli.

TCD is possibly effective in documenting changes in flow velocities and CO_2 reactivity in patients who undergo CABG (Type C, Class III evidence). TCD is probably useful for the detection and monitoring of cerebral microemboli in patients undergoing CABG (Type B, Class II to III evidence). Data are presently insufficient regarding the clinical utility of this information (Type U).

Cerebral thrombolysis. Occlusions of the MCA may recanalize according to TCD criteria in 65 to 89% of patients within 1 to 3 weeks after stroke onset.[30,33,78,79] Sonographic findings that may be observed during spontaneous or induced recanalization of acute MCA occlusions vary according to the pattern and extent of occlusive lesion(s), extent of collateral circulation, rapidity of recanalization, occurrence of reocclusion, and intensity of TCD monitoring.[80-83] For example, TCD can differentiate between tandem extracranial ICA/MCA lesions and isolated MCA occlusions; the former may have collateral flow patterns and stenotic terminal ICA signals.[84] Sensitivity and specificity of TCD for detection of angiographic recanalization are generally good to excellent for complete occlusion, partial occlusion, and recanalization, although the sensitivity for complete occlusion is low.[80] Recanalization within 5 to 8 hours, especially when accompanied by good collaterals, has been associated with more rapid and improved outcomes.[78,81] The presence of residual flow signals such as systolic spikes, blunted or dampened waveforms, thrombus vibration, microembolic signals, or transient flow changes before thrombolysis is associated with an increased likelihood of complete recanalization.[85] A recent TCD study of patients with MCA occlusion treated with IV thrombolysis[82] showed normal restoration of flow in 58% of patients with dramatic recovery and only 14% of patients without dramatic recovery. One recent 1:2 case-control study of cardioembolic stroke[86] showed that use of IV recombinant tissue plasminogen activator therapy was associated with significantly higher 6-hour recanalization rate (66 vs 15%) and significantly reduced infarct volume (50.2 ± 40.3 vs 124.8 ± 81.6 cm^3) compared with controls. A recent small randomized trial[87] comparing IV thrombolysis ($n = 14$) and IV thrombolysis with continuous ultrasonic monitoring ($n = 11$) in acute MCA occlusion suggested a higher grade of recanalization at 1 hour and improved clinical outcome at 90 days in patients receiving continuous ultrasonic monitoring. Issues of the use of TCD for hyperacute ischemic stroke patient selection for, as well as efficacy and safety of ultrasonic monitoring of, cerebral thrombolysis are currently being explored in the Combined Lysis of Thrombus in Brain Ischemia with Transcranial Ultrasound and Systemic TPA (CLOTBUST) trial.

TCD is probably useful for monitoring thrombolysis of acute MCA occlusions (Type B, Class II to III evidence). Present data are insufficient to either define the optimal frequency of TCD monitoring for clot dissolution and enhanced recanalization or to influence therapy (Type U).

Monitoring in the neurology/neurosurgery intensive care unit. *SAH.* Delayed narrowing or vasoconstriction of intracerebral arteries, or vasospasm (VSP), occurs in diverse clinical settings. In the Timing of Aneurysm Surgery Study, VSP-related ischemic neurologic deficits were the major cause of mortality (7.2%) and morbidity (6.3%) in survivors of aneurysmal SAH.[88] Angiographic VSP, detectable in 21 to 70% of patients with aneurysmal SAH, can occur in all intracranial arteries, either proximally or distally. Clinical syndromes believed to be attributable to severe, flow-reducing VSP in each intracranial vessel have been described. There is an inverse relation between cerebral blood flow, cerebral blood flow velocities, and age.[89,90] Neurologic deterioration in this setting may be associated with a number of disorders, and the presence of large-vessel angiographic VSP does not always lead to neurologic deterioration.

Spontaneous SAH. In general, TCD flow velocity findings in the MCA correlate well with clinical grade, CT localization of SAH clot, and the time course of angiographic VSP. However, these correlations are imperfect. There is a significant direct correlation between VSP severity after spontaneous SAH (sSAH) and flow velocities in cerebral arteries, although anatomic and technical factors weaken the association for the intracranial ICA and ACA.[91-98] For the MCA, flow velocities of <120 or >200 cm/s, a rapid rise in flow velocities, or a higher Lindegaard (V_{MCA}/V_{ICA}) ratio (6 ± 0.3) reliably predict the absence or presence of clinically significant angiographic MCA VSP, although prediction of neurologic deterioration is problematic.[91,92] Similar data for the other intracranial vessels are not available. A variety of factors such as technical issues, vessel anatomy, age, intracranial pressure (ICP), mean arterial

blood pressure, hematocrit, arterial CO_2 content, collateral flow patterns, and response to therapeutic interventions influence flow velocities and must be taken into account when interpreting TCD results in this setting.

The sensitivity and specificity of TCD vs cerebral angiography for the detection of VSP after sSAH in the proximal portions of each intracranial artery have been summarized. In a recent meta-analysis,[91] only 5 of 26 evaluable TCD studies[93-97] met at least 7 of 10 criteria for methodologically high-quality studies. In general, data vary by vessel and by diagnostic criteria, disease prevalence, and timing of correlative angiography. Specific causes of false-positive and false-negative TCD examinations have been identified for each intracranial vessel[95-99] and their impact on the approach to test performance and interpretation described. TCD flow velocity criteria appear most reliable for detecting angiographic MCA VSP and BA VSP. The specificity of TCD can be optimized by increasing the flow velocity criteria and sensitivity by the timing of the angiographic correlation for the diagnosis of VSP.[94,95]

TCD is useful in monitoring the temporal course of angiographic VSP after sSAH. Although no adequate study has been conducted, TCD is thought to be valuable in the day-to-day evaluation of sSAH patients in VSP and to assess the effect and durability of neuroradiologic interventions.[100,101] TCD has been used to detect angiographic VSP following prophylactic transluminal balloon angioplasty in sSAH patients at high risk of developing VSP,[102] as a noninvasive surrogate endpoint, or to demonstrate biologic effects of treatments for vasoconstriction or VSP in uncontrolled trials of pharmacologic therapies for eclampsia and sSAH.[103-106] Data are insufficient to make a recommendation regarding the use and method(s) of autoregulation testing for prediction of the risk of delayed cerebral ischemia. In general, TCD is not useful for the detection of VSP directly affecting the convexity or vertically oriented branches of the intracranial arteries distal to the basal cisterns,[98,99] although the presence of VSP at these sites may be inferred in some cases by indirect Doppler waveform observations (e.g., decreased diastolic flow, increased pulsatility, side-to-side differences in pulsatility indexes, etc.).

TCD is useful for the detection and monitoring of angiographic VSP in the basal segments of the intracranial arteries, especially the MCA and BA, following sSAH (Type A, Class I to II evidence). More data are needed to show if TCD affects clinical outcomes in this setting (Type U).

Traumatic SAH. CT evidence of SAH following closed head injury occurs in 4 to 63% of patients.[107-112] Patients with traumatic SAH (tSAH) may develop delayed arterial narrowing consistent with VSP, with the site of severe VSP correlating with the site of tSAH. The VSP associated with tSAH is more common with massive bleeding and may lead to focal neurologic deficits in any vascular distribution. Closed head injury patients with tSAH or hemodynamically significant VSP with reduced cerebral blood flow have a significantly worse prognosis (death, persistent vegetative state, severe disability) than patients without tSAH or VSP.[107-109,112]

There are a number of studies of TCD monitoring of patients with severe head injury.[108-112] Patients with increasing severity of head injury will have significantly lower MCA velocities at hospital admission.[109] VSP has been defined in various ways, but the sensitivity and specificity of TCD vs angiography for the detection of VSP in intracranial arteries following closed head injury have not been reported. Hemodynamically significant VSP, as defined by abnormal MCA velocities ($\geq$120 cm/s), V_{MCA}/V_{ICA} of $>$3.00, MCA spasm index (ratio of MCA flow velocities to hemispheric cerebral blood flow) of $>$3.4, BA velocities of $\geq$90 cm/s, or BA spasm index (ratio of BA flow velocities to global cerebral blood flow) of $>$2.5, has been associated with a significantly worse outcome (especially for the spasm indexes).[112] In the German tSAH Study,[111] patients receiving nimodipine tended to have lower MCA velocities. Monitoring with TCD and jugular bulb oxygen saturation may be used to optimize ventilatory and pharmacologic[108] management of patients with severe closed head injury. Persistently low MCA velocities have been associated with early ($<$72 hours) death.[108]

TCD is probably useful for the detection of VSP and cerebral hemodynamic impairment following tSAH (Type B, Class I to III evidence). Data on sensitivity, specificity, and predictive value of TCD for VSP after tSAH are needed. Data are insufficient regarding how use of TCD affects clinical outcomes after tSAH (Type U).

Increased ICP and cerebral circulatory arrest. There is a qualitative relationship between progressive increases in ICP and the evolution of abnormal TCD waveforms, assuming a constant arterial CO_2 content and a constant degree of distal vasoconstriction. Pulsatility changes occur when cerebral perfusion pressure is $<$70 mm Hg. The earliest sign of increased ICP is increased pulsatility, followed by progressive reduction in diastolic flow velocities and reduction in mean flow velocities. As regional or generalized ICP elevation becomes increasingly extreme, diastolic flow reaches zero, followed by an alternating flow pattern with retrograde diastolic flow, disappearance of diastolic flow, appearance of small systolic spikes, and eventually no flow. Once the reverberating flow pattern appears, cerebral blood flow disappears on angiography and brain death is likely. Evolutionary changes may occur over a period of minutes to hours.[1,113-117]

Brain death is a clinical diagnosis that can be supported by TCD evidence of absent cerebral blood flow (zero net flow velocity) at all insonation sites. Diagnostic criteria for cerebral circulatory arrest/brain death by TCD have been published, with sensitivity and specificity of 91 to 100% and 97 to 100%, respectively.[113-116] The specificity is imperfect as ab-

sence of MCA flow may be transient or BA flow may still be present; when systolic spikes are present in multiple intracranial compartments, recovery is unlikely.[115] The most stringent criteria require similar waveform patterns to be present in the extracranial common carotid artery, ICA, and VA.[117] TCD is especially helpful in patients with suspected brain death who have loss of brainstem function due to isolated brainstem lesions or who received sedative or paralytic agents that render clinical examination or interpretation of EEG difficult. TCD can confirm the clinical diagnosis of brain death.[118] TCD is a useful adjunct test for the evaluation of cerebral circulatory arrest associated with brain death (Type A, Class II evidence).

TCCS or imaging TCD. TCCS is a relatively new, bedside noninvasive technique that shows a real-time two-dimensional depiction of cerebral parenchymal and intracranial vascular structures.[119-125] Compared with conventional TCD, there is more accurate demonstration of vascular anatomy, because imaging of smaller arterial branches and venous structures is feasible. Depending on the vessel, the uncorrected insonation angle may be as high as 73°.[120,121,124] As a result, angle-corrected flow velocities may be as much as 25 to 30% higher than non-angle-corrected flow velocities.[120-122,124] Age-specific normative data have been published.[124,126,127] In Caucasian atherosclerotic patients over age 60, vessel detection rates are lower and blood flow velocities are higher in women.[123] In general, flow velocity measurements are highly reproducible. However, errors in flow velocity measurement in two dimensions may still occur because of the three-dimensional course of intracranial arteries and the possibility of large insonation angles.[121] Use of the lateral frontal bone window may help with detection of posterior communicating artery flow and flow direction.[128]

As with conventional TCD, a major limitation of TCCS is insufficient transtemporal ultrasound beam penetration due to hyperostosis of the skull.[119-126] Transpulmonary echocontrast agents (ECA) increase the Doppler signal intensity and improve the signal-to-noise ratio for transcranial insonation.[129] The use of an ECA enhances the ability of TCCS to visualize the number and length of basal cerebral arteries and second- or third-order branches of major cerebral arteries,[126] particularly in patients with poor transtemporal windows.[130-135] The use of ECA may increase the peak systolic velocities in a cerebral artery segment by as much as 26 ± 10% and produce "bubble noise."[136,137] However, if non-contrast-enhanced TCCS does not reveal any intracranial structures such as the midbrain or any cerebral artery, then contrast-enhanced TCCS will not be diagnostically conclusive.[130,133] A recent power-based TCCS study of 687 consecutive patients[138] showed that an indication for use of an ECA was present in 8.8% of cases. There was a diagnostic result in 75% of cases during transtemporal insonation and 81% of cases during transforaminal insonation. ECA are currently used in clinical practice in Germany but have not been approved by the U.S. Food and Drug Administration.

Ischemic cerebrovascular disease. In patients with ischemic cerebrovascular disease, contrast-enhanced TCCS may be useful in several ways. Morphologic data suggest that the threshold arterial diameter allowing for functional collateral flow in the circle of Willis is between 0.4 and 0.6 mm, which can be detected by TCCS.[139] TCCS can detect presence and direction of collateral flow in the anterior (ACoA) and posterior (PCoA) communicating arteries in patients with hemodynamically significant (typically ≥80%) ICA stenosis or occlusion, with improvement to as much as 96% diagnostic confidence following use of ECA.[134-140] Sensitivity and specificity for the detection of ACoA and PCoA collateral flow are good to excellent.[141] Compared with the temporal bone window, use of the lateral frontal bone window appears to increase the detection of intracranial cross-flow patterns via the PCoA.[128]

Limited data suggest that intracranial stenoocclusive disease,[26,130-133] including >50% diameter reduction stenosis[27] or distinction between vessel patency or occlusion with reduced flow velocity,[132,133] can be detected more reliably with contrast-enhanced TCCS than with TCD. TCCS can demonstrate areas of parenchymal hypoechogenicity in the MCA distribution suggestive of ischemic cerebral infarction shown on brain CT scan, accompanied by abnormal blood flow velocity pattern, with fair to good sensitivity and specificity.[141,142] Spontaneous[131,135,141] and thrombolytic therapy-induced[135,142] recanalization, as compared with DSA, MRA, or CTA in small numbers of patients,[142] can be monitored by serial TCCS examinations, with recanalization being more common in patients treated with thrombolytic therapy.[135] Severe neurologic deficits and large MCA territory ischemic infarctions have been associated with sonographic signs of MCA occlusion or decreased MCA flow velocities within 12 hours of stroke onset,[133] whereas a patent MCA without reduced MCA flow velocities may be predictive of early clinical improvement.[132] (Contrast-enhanced) TCCS is probably useful in the evaluation and monitoring of patients with ischemic cerebrovascular disease (Type B, Class II to IV evidence).

Hemorrhagic cerebrovascular disease. Most of the experience with (contrast-enhanced) TCCS in hemorrhagic cerebrovascular disease is in patients with aneurysmal SAH.[143-148] A marked increase in the echodensity of the basal cisterns or ventricular system indicates the presence of blood in the subarachnoid or intraventricular space, respectively.[147] TCCS can detect 76 to 91% of nonthrombosed intracranial aneurysms of ≥6 mm in size[144-147]; use of ECA or power Doppler may increase the rate of detection, including aneurysms <5 mm in size.[146,147] TCCS may detect VSP in major branches of the circle of Willis following SAH.[143,148] Limited data suggest that sensitivity and specificity of TCCS for detection of intracranial ICA and MCA VSP are excellent.[148] However,

no data exist to compare the utility of (contrast-enhanced) TCCS with conventional TCD in this setting.

Parenchymal hematomas larger than 1 mL in size may be detected by TCCS, although smaller or cortical lesions may be missed.[149] Acute (<5 days old) hematomas may appear as echodense lesions when compared with surrounding tissues; evolutionary changes in ICH characteristics can be documented on serial scans. Complications of ICH such as intraventricular extension, hydrocephalus, and increased ICP can also be demonstrated. Limited data suggest that for ICH, TCCS has excellent sensitivity, specificity, positive predictive value, and negative predictive value in patients with adequate transtemporal windows.[149]

(Contrast-enhanced) TCCS is probably useful in the evaluation and monitoring of patients with aneurysmal SAH or intracranial ICA/MCA VSP following SAH (Type B, Class II to III evidence). Data are presently insufficient regarding the use of TCCS to replace CT for diagnosis of ICH (Type U).

Other indications. There are insufficient data to support the routine clinical use of TCD/TCCS for other indications including migraine, cerebral venous thrombosis, monitoring during cerebral angiography, evaluation of arteriovenous malformations, and evaluation of cerebral autoregulation in other settings (Type U recommendation). For discussion of these and other possible indications for the use of TCD, the interested reader is referred to other sources.[1]

Summary and conclusions

1. Settings in which TCD is able to provide information and in which its clinical utility is established.
   a. Screening of children aged 2 to 16 years with sickle cell disease for assessing stroke risk (Type A, Class I), although the optimal frequency of testing is unknown (Type U).
   b. Detection and monitoring of angiographic VSP sSAH (Type A, Class I-II). More data are needed to show if its use affects clinical outcomes (Type U).
2. Settings in which TCD is able to provide information, but in which its clinical utility, compared with other diagnostic tools, remains to be determined.
   a. Intracranial steno-occlusive disease. TCD is probably useful (Type B, Class II to III) for the evaluation of occlusive lesions of intracranial arteries in the basal cisterns (especially the ICA siphon and MCA). The relative value of TCD compared with MRA or CTA remains to be determined (Type U). Data are insufficient to recommend replacement of conventional angiography with TCD (Type U).
   b. Cerebral circulatory arrest (adjunctive test in the determination of brain death). If needed, TCD can be used as a confirmatory test, in support of a clinical diagnosis of brain death (Type A, Class II).
3. Settings in which TCD is able to provide information, but in which its clinical utility remains to be determined.
   a. Cerebral thrombolysis. TCD is probably useful for monitoring thrombolysis of acute MCA occlusions (Type B, Class II to III). More data are needed to assess the frequency of monitoring for clot dissolution and enhanced recanalization and to influence therapy (Type U).
   b. Cerebral microembolism detection. TCD monitoring is probably useful for the detection of cerebral microembolic signals in a variety of cardiovascular/cerebrovascular disorders/procedures (Type B, Class II to IV). Data do not support the use of this TCD technique for diagnosis or monitoring response to antithrombotic therapy in ischemic cerebrovascular disease (Type U).
   c. CEA. TCD monitoring is probably useful to detect hemodynamic and embolic events that may result in perioperative stroke during and after CEA in settings where monitoring is felt to be necessary (Type B, Class II to III).
   d. CABG surgery. TCD monitoring is probably useful (Type B, Class II to III) during CABG for detection of cerebral microemboli. TCD is possibly useful to document changes in flow velocities and CO_2 reactivity during CABG surgery (Type C, Class III). Data are insufficient regarding the clinical impact of this information (Type U).
   e. VMR testing. TCD is probably useful (Type B, Class II to III) for the detection of impaired cerebral hemodynamics in patients with severe (>70%) asymptomatic extracranial ICA stenosis, symptomatic or asymptomatic extracranial ICA occlusion, and cerebral small-artery disease. Whether these techniques should be used to influence therapy and improve patient outcomes remains to be determined (Type U).
   f. VSP after tSAH. TCD is probably useful for the detection of VSP following tSAH (Type B, Class III), but data are needed to show its accuracy and clinical impact in this setting (Type U).
   g. TCCS. TCCS is possibly useful (Type C, Class III) for the evaluation and monitoring of space-occupying ischemic MCA infarctions. More data are needed to show if it has value vs CT and MRI scanning and if its use affects clinical outcomes (Type U).
4. Settings in which TCD is able to provide information, but in which other diagnostic tests are typically preferable.
   a. Right-to-left cardiac shunts. Whereas TCD is useful for detection of right-to-left cardiac and extracardiac shunts (Type A, Class II), TEE is superior, as it can provide direct information regarding the anatomic site and nature of the shunt.

b. Extracranial ICA stenosis. TCD is possibly useful for the evaluation of severe extracranial ICA stenosis or occlusion (Type C, Class II to III), but, in general, carotid duplex and MRA are the diagnostic tests of choice.
c. Contrast-enhanced TCCS. (Contrast-enhanced) TCCS may provide information in patients with ischemic cerebrovascular disease and aneurysmal SAH (Type B, Class II to IV). Its clinical utility vs CT scanning, conventional angiography, or nonimaging TCD is unclear (Type U).

Recommendations for future research

1. Ischemic cerebrovascular disease.
   a. Sickle cell disease. The optimal frequency for screening children between the ages of 2 and 16 years needs to be determined. Data are needed to assess the value of TCD in the evaluation of adults with sickle cell disease and its impact, if any, on selection of treatment and prognosis.
   b. Intracranial steno-occlusive disease. More data are needed to define the ability of TCD to detect ≥50% stenosis of major basal intracranial arteries vs MRA and CTA. Once MRA and CTA are validated, the relative value of each technique for specific vascular lesions that may influence patient management must be determined. The ability of TCD to predict outcome in vertebrobasilar distribution stroke, if any, requires study. The value of TCD in the prediction of hemorrhagic transformation of ischemic infarction needs confirmation in well-designed studies of patients who do and do not receive anticoagulation or thrombolysis.
   c. Extracranial ICA stenosis. The clinical utility of TCD's ability to detect impaired cerebral hemodynamics distal to high-grade extracranial ICA stenosis or occlusion and assist with stroke risk assessment needs confirmation and evaluation in randomized clinical trials. In patients with symptomatic ICA occlusion, it would be useful to directly compare TCD/VMR testing with PET to see if TCD would be valuable to select and serially monitor patients for extracranial-to-intracranial bypass surgery. In patients with asymptomatic high-grade ICA stenosis, it would be useful to learn if TCD assessment of VMR or microembolic signal detection can improve selection of patients for CEA or angioplasty.
2. Perioperative and periprocedural monitoring.
   a. Cerebral microembolization. The ability of TCD to better distinguish between the various types of microembolic signals needs to be enhanced. Clinical utility in specific disease states should be defined.
   b. CEA. The incremental value of TCD monitoring compared with other intraoperative monitoring procedures (EEG, evoked potentials, stump pressures, cerebral blood flow) needs further study.
   c. CABG surgery. More data are needed to show if TCD predicts the occurrence of stroke or neurocognitive impairment following CABG or is useful as a biomarker or surrogate endpoint for clinical trials of neuroprotective agents or new surgical techniques.
   d. Cerebral thrombolysis. The value of TCD in monitoring thrombolytic therapy (IV and intra-arterial) and other recanalizing techniques needs to be shown in clinical trials. Data from such studies might help in determining the need for further interventions and predicting the outcome of treated and nontreated patients. In addition, studies should be done to determine if thrombolysis can be enhanced with specific frequency(ies) of transcranial ultrasound.
3. Monitoring in the neurology/neurosurgery intensive care unit.
   a. SSAH. More data are needed on the sensitivity and specificity of TCD in the detection of angiographic VSP in different age groups, as diagnostic criteria (like normative data) may vary with age. It remains to be shown how use of TCD affects clinical outcomes. The ability of specific TCD measurements to predict long-term outcome from SAH requires study.
   b. TSAH. Data on the sensitivity and specificity of TCD for detection of angiographic VSP in this setting are needed. More data are needed to show the clinical utility and predictive power of TCD.
   c. Contrast-enhanced TCCS. The incremental value of (contrast-enhanced) TCCS in diverse settings of ischemic and hemorrhagic cerebrovascular disease, in comparison with TCD, CT, CTA, MRI, MRA, and conventional angiography, needs to be confirmed. Whether (contrast-enhanced) TCCS can assist stroke and neuro–intensive care unit clinicians in the monitoring of reperfusion techniques or selection of patients with severe MCA territory infarction for clinical trials of aggressive, putative beneficial, or life-saving therapies remains to be determined.

Disclaimer This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurology problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

Appendix 1

The Therapeutic and Technology Assessment Subcommittee members are Douglas S. Goodin, MD (chair); Yuen T. So, MD, PhD (vice-chair); Carmel Armon, MD, MHS; Richard M. Dubinsky, MD; Mark Hallett, MD; David Hammond, MD; Chung Y. Hsu, MD, PhD; Andres M. Kanner, MD; David Lefkowitz, MD; Janis Miyasaki, MD; Michael A. Sloan, MD, MS; and James C. Stevens, MD.

Appendix 2

Additional material related to this article can be found on the AAN web site. Visit www.aan.com/professionals/practice/index.cfm to view the entire guideline.

References

1. Babikian VL, Feldmann E, Wechsler LR, et al. Transcranial Doppler ultrasonography: year 2000 update. J Neuroimag 2000;10:101–115.
2. Assessment of brain SPECT. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 1996;46:278–285.
3. Goodin DS, Edlund W. Process for developing technology assessments. American Academy of Neurology Therapeutics and Technology Subcommittee, 1999:1–35.
4. Adams RJ, McKie VC, Carl EM, et al. Long-term stroke risk in children with sickle cell disease screened with transcranial Doppler. Ann Neurol 1997;43:699–704. Class II
5. Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle anemia and abnormal results on transcranial Doppler ultrasonography. N Engl J Med 1998;339:5–11. Class I
6. Job FP, Ringelstein EB, Grafen Y, et al. Comparison of transcranial contrast Doppler sonography and transesophageal contrast echocardiography for the detection of patent foramen ovale in young stroke patients. Am J Cardiol 1994;75:381–384. Class II
7. Nemec JJ, Marwick TH, Lorig RJ, et al. Comparison of transcranial Doppler ultrasound and transesophageal contrast echocardiography in the detection of interatrial right-to-left shunts. Am J Cardiol 1991;68: 1498–1502. Class II
8. Cabanes L, Mas JL, Cohen A, et al. Atrial septal aneurysm and patent foramen ovale as risk factors for cryptogenic stroke in patients less than 55 years of age: a study using transesophageal echocardiography. Stroke 1993;24:1865–1873. Class II
9. Mas J-L, Arquizan C, Lamy C, et al., for the Patent Foramen Ovale and Atrial Septal Aneurysm Study Group. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. N Engl J Med 2001;345:1740–1746. Class II
10. Albert A, Muller HR, Hetzel A. Optimized transcranial Doppler technique for the diagnosis of cardiac right-to-left shunts. J Neuroimag 1997;7:159–163. Class II
11. Schwarze JJ, Sander D, Kukla C, et al. Methodological parameters influence the detection of right-to-left shunts by contrast transcranial Doppler ultrasonography. Stroke 1999;30:1234–1239. Class II
12. Droste DW, Lakemeier S, Wichter T, et al. Optimizing the technique of contrast transcranial Doppler ultrasound in the detection of right-to-left shunts. Stroke 2002;33:2211–2216. Class III
13. Sacco RL, Kargman D, Gu Q, Zamanillo MC. Race–ethnicity and determinants of intracranial atherosclerotic cerebral infarction: the Northern Manhattan Stroke Study. Stroke 1995;26:14–20. Class II
14. 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. Class III
15. Rorick MB, Nichols FT, Adams RJ. Transcranial Doppler correlation with angiography in detection of intracranial stenosis. Stroke 1994;25: 1931–1934. Class II
16. Ley–Pozo J, Ringelstein EB. Noninvasive detection of occlusive disease of the carotid siphon and middle cerebral artery. Ann Neurol 1990;28: 640–647. Class II
17. DeBray JM, Joseph PA, Jeanvoine H, et al. Transcranial Doppler evaluation of middle cerebral artery stenosis. J Ultrasound Med 1988; 7:611–616. Class II
18. Babikian V, Sloan MA, Tegeler CH, et al. Transcranial Doppler validation pilot study. J Neuroimag 1993;3:242–249. Class II
19. Mull M, Aulich A, Hennerici M. Transcranial Doppler ultrasonography versus arteriography for assessment of the vertebrobasilar circulation. J Clin Ultrasound 1990;18:539–549. Class II
20. Zanette EM, Fieschi C, Bozzao L, et al. Comparison of cerebral angiography and transcranial Doppler sonography in acute stroke. Stroke 1989;20:899–903. Class II
21. Camerlingo M, Casto L, Censori B, et al. Transcranial Doppler in acute ischemic stroke of the middle cerebral artery territories. Acta Neurol Scand 1993;88:108–111. Class II
22. Camerlingo M, Casto L, Censori B, et al. Prognostic use of ultrasonography in acute non-hemorrhagic carotid stroke. Ital J Neurol Sci 1996; 17:215–218. Class II
23. Baracchini C, Manara R, Ermani M, Meneghetti G. The quest for early predictors of stroke evolution. Can TCD be a guiding light? Stroke 2000;31:2942–2947. Class III
24. Wong KS, Li H, Chan YL, et al. Use of transcranial Doppler ultrasound to predict outcome in patients with intracranial large-artery occlusive disease. Stroke 2000;31:2641–2647. Class III
25. Kushner MJ, Zanette EM, Bastianello S, et al. Transcranial Doppler in acute hemispheric brain infarction. Neurology 1991;41:109–113. Class II
26. Baumgartner RW, Mattle HP, Schroth G. Assessment of greater than/equal to 50% and less than 50% intracranial stenoses by transcranial color-coded duplex sonography. Stroke 1999;30:87–92. Class II
27. Schwarze JJ, Babikian VL, DeWitt LD, et al. Longitudinal monitoring of intracranial arterial stenoses with transcranial Doppler ultrasonography. J Neuroimag 1994;4:182–187. Class III
28. Arenillas JF, Molina CA, Montaner J, et al. Progression and clinical recurrence of symptomatic middle cerebral artery stenosis: a long-term follow-up transcranial Doppler ultrasound study. Stroke 2001;32: 2898–2904. Class III
29. Wong KS, Li H, Lam WWM, 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. Class III
30. Fieschi C, Argentino C, Lenzi GL, Sacchetti ML, Toni D, Bozzao L. Clinical and instrumental evaluation of patients with ischemic stroke within the first six hours. Ital J Neurol Sci 1989;91:311–321. Class II
31. Demchuk AM, Christou I, Wein TH, et al. Accuracy and criteria for localizing arterial occlusion with transcranial Doppler. J Neuroimag 2000;10:1–12. Class II
32. Toni D, Fiorelli M, Zanette EM, et al. Early spontaneous improvement and deterioration of ischemic stroke patients. Stroke 1998;29:1144–1148. Class II
33. Alexandrov AV, Black SE, Ehrlich LE, Caldwell CB, Norris JW. Predictors of hemorrhagic transformation occurring spontaneously and on anticoagulants in patients with acute ischemic stroke. Stroke 1997;28: 1198–1202. Class II
34. Molina CA, Montaner J, Abilleira S, et al. Timing of spontaneous recanalization and risk of hemorrhagic transformation in acute cardioembolic stroke. Stroke 2001;32:1079–1084. Class III
35. Wilterdink JL, Feldmann E, Furie KL, Bragoni M, Benavides JG. Transcranial Doppler ultrasound battery reliably identifies severe internal carotid artery stenosis. Stroke 1997;28:133–136. Class III
36. Can U, Furie KL, Suwanwela N, et al. Transcranial Doppler ultrasound criteria for hemodynamically significant internal carotid artery stenosis based on residual lumen diameter calculated from en bloc endarterectomy specimens. Stroke 1997;28:1966–1971. Class III
37. Christou I, Felberg RA, Demchuk AM, et al. A broad diagnostic battery for bedside transcranial Doppler to detect flow changes with internal carotid artery stenosis or occlusion. J Neuroimag 2001;11:236–242. Class II–III
38. Ringelstein EB, Van Eyck S, Mertens I. Evaluation of cerebral vasomotor reactivity by various vasodilating stimuli: comparison of CO_2 to acetazolamide. J Cereb Blood Flow Metab 1992;12:162–168. Class III
39. Markus H, Cullinane M. Severely impaired cerebrovascular reactivity predicts stroke and TIA risk in patients with carotid artery stenosis and occlusion. Brain 2001;124:457–467. Class II–III
40. Russell D, Dybevold S, Kjartansson O, et al. Cerebral vasoreactivity and blood flow before and 3 months after carotid endarterectomy. Stroke 1990;21:1029–1032. Class II–III
41. Muller M, Schimrigk K. Vasomotor reactivity and pattern of collateral blood flow in severe occlusive carotid artery disease. Stroke 1996;27: 296–299. Class III
42. Vernieri F, Pasqualetti P, Passarelli F, Rossini PM, Silvestrini M. Outcome of carotid artery occlusion is predicted by cerebrovascular reactivity. Stroke 1999;30:593–598. Class II
43. Silvestrini M, Vernieri F, Pasqualetti P, et al. Impaired cerebral vasoreactivity and risk of stroke in patients with asymptomatic carotid artery stenosis. JAMA 2000;283:2122–2127. Class I
44. Vernieri F, Pasqualetti P, Matteis M, et al. Effect of collateral blood flow and cerebral vasomotor reactivity on the outcome of carotid artery occlusion. Stroke 2001;32:1552–1558. Class II–III
45. Settakis G, Lengyel A, Molnar C, et al. Transcranial Doppler study of the cerebral hemodynamic changes during breath-holding and hyperventilation tests. J Neuroimag 2002;12:252–258. Class III
46. Ratsep T, Asser T. Cerebral hemodynamic impairment after aneurysmal subarachnoid hemorrhage as evaluated using transcranial Doppler ultrasonography: relationship to delayed cerebral ischemia and clinical outcome. J Neurosurg 2001;95:393–401. Class III
47. Derdeyn CP, Grubb RL Jr, Powers WJ. Cerebral hemodynamic impairment: methods of measurement and association with stroke risk. Neurology 1999;53:251–259.
48. Markus HS, Ackerstaff R, Babikian V, et al. Intercenter agreement in reading Doppler embolic signals: a multicenter international study. Stroke 1997;28:1307–1310. Class II–III
49. Ringelstein EB, Droste DW, Babikian VL, et al. Consensus on microembolus detection by TCD: International Consensus Group on Microembolus Detection. Stroke 1998;29:725–729. Class IV

50. Goertler M, Blaser T, Krueger S, et al. Cessation of embolic signals after antithrombotic prevention is related to reduced risk of recurrent arterioembolic transient ischaemic attack and stroke. J Neurol Neurosurg Psychiatry 2002;72:338–342. Class III
51. Molloy J, Markus HS. Asymptomatic embolization predicts stroke and TIA risk in patients with carotid artery stenosis. Stroke 1999;30: 1440–1443. Class III
52. Stork JL, Kimura K, Levi CR, et al. Source of microembolic signals in patients with high-grade carotid stenosis. Stroke 2002;33:2014–2018. Class III
53. Spencer MP. Transcranial Doppler monitoring and the causes of stroke from carotid endarterectomy. Stroke 1997;28:685–691. Class III
54. Spencer M, Thomas GI, Moehring MA. Relation between middle cerebral artery blood flow velocity and stump pressure during carotid endarterectomy. Stroke 1992;23:1439–1445. Class II
55. Arnold M, Sturzenegger M, Schaffler L, Seiler RW. Continuous intraoperative monitoring of middle cerebral artery blood flow velocities and electroencephalography during carotid endarterectomy. A comparison of the two methods to detect cerebral ischemia. Stroke 1997;28: 1345–1350. Class I
56. Jansen C, Vriens EM, Eikelboom BC, et al. Carotid endarterectomy with transcranial Doppler and electroencephalographic monitoring. A prospective study in 130 operations. Stroke 1993;24:665–669. Class III
57. Barzo P, Voros E, Bodosi M. Use of transcranial Doppler sonography and acetazolamide test to demonstrate changes in cerebrovascular reserve capacity following carotid endarterectomy. Eur J Vasc Endovasc Surg 1996;11:83–89. Class II
58. Hartl WH, Janssen I, Furst H. Effect of carotid endarterectomy on patterns of cerebrovascular reactivity in patients with unilateral carotid stenosis. Stroke 1994;25:1952–1957. Class III
59. Gaunt ME, Martin PJ, Smith JL, et al. Clinical relevance of intraoperative embolization detected by transcranial Doppler ultrasonography during carotid endarterectomy: a prospective study of 100 patients. Br J Surg 1994;81:1435–1439. Class II
60. Levi CR, O'Malley HM, Fell G, et al. Transcranial Doppler detected cerebral microembolism following carotid endarterectomy. High microembolic signal loads predict postoperative cerebral ischemia. Brain 1997;120:621–629. Class III
61. Hayes PD, Lloyd AJ, Lennard N, et al. Transcranial Doppler-directed Dextran-40 therapy is a cost-effective method of preventing carotid thrombosis after carotid endarterectomy. Eur J Vasc Endovasc Surg 2000;19:56–61. Class I
62. Jansen C, Ramos LMP, van Heesewijk JPM, Moll FL, van Gijn J, Ackerstaff RGA. Impact of microembolism and hemodynamic changes in the brain during carotid endarterectomy. Stroke 1994;25:992–997. Class III
63. Ackerstaff RGA, Moons KGM, van de Vlasakker CJW, et al. Association of intraoperative transcranial Doppler monitoring variables with stroke from carotid endarterectomy. Stroke 2000;31:1817–1823. Class III
64. Lennard N, Smith JL, Gaunt ME, et al. A policy of quality control assessment helps to reduce the risk of intraoperative stroke during carotid endarterectomy. Eur J Vasc Endovasc Surg 1999;17:234–240. Class II
65. Stork JL, Levi CR, Chambers BR, Abbott AL, Donnan GA. Possible determinants of early microembolism after carotid endarterectomy. Stroke 2002;33:2082–2085. Class III
66. Lennard N, Smith JL, Dumville J, et al. Prevention of postoperative thrombotic stroke after carotid endarterectomy: the role of transcranial Doppler ultrasound. J Vasc Surg 1997;26:579–584. Class III
67. Kaposzta Z, Baskerville PA, Madge D, et al. L-Arginine and *S*-nitrosoglutathione reduce embolization in humans. Circulation 2001;103:2371–2375. Class II–III
68. Roach GW, Kanchuger M, Mangano CM, et al., for the Multicenter Study of Perioperative Ischemia Research Group and Education Foundation Investigators. Adverse cerebral outcomes after coronary artery surgery. N Engl J Med 1996;335:1857–1863. Class II
69. Newman MF, Kirchner JL, Phillips–Bute B, et al., for the Neurologic Outcome Research Group and the Cardiothoracic Anesthesiology Research Endeavors Investigators. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med 2001;344:395–402. Class II–III
70. Newman MF, Wolman R, Kanchuger M, et al., and participants in the Multicentre Study of Perioperative Ischemia (McSPI) Research Group. Multicenter preoperative stroke index for patients undergoing coronary artery bypass surgery. Circulation 1996;94(suppl II):II74–II80. Class II–III
71. McKhann GM, Goldsborough MA, Borowicz LM, et al. Predictors of stroke risk in coronary artery bypass patients. Ann Thor Surg 1997; 63:516–521. Class II–III
72. McKhann GM, Grega MA, Borowicz LM, et al. Encephalopathy and stroke after coronary artery bypass grafting: incidence, consequences and prediction. Arch Neurol 2002;59:1422–1428. Class III
73. Barbut D, Yao FS, Hager DN, et al. Comparison of transcranial Doppler ultrasonography and transesophageal echocardiography to monitor emboli during coronary artery bypass surgery. Stroke 1996;27:87–90. Class III
74. Pugsley W, Klinger L, Paschalis C, Treasure T. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. Stroke 1994;25:1393–1399. Class III
75. Borger MA, Taylor RL, Weisel RD, et al. Decreased cerebral emboli during distal aortic arch cannulation: a randomized clinical trial. J Cardiovasc Thorac Surg 1999;118:740–745. Class II–III
76. Lloyd CT, Ascione R, Underwood MJ, et al. Serum S-100 protein release and neuropsychological outcome during coronary revascularization on the beating heart: a prospective randomized study. J Cardiovasc Thorac Surg 2000;119:148–154. Class II
77. Bowles BJ, Lee JD, Dang CR, et al. Coronary artery bypass performed without the use of cardiopulmonary bypass is associated with reduced cerebral microemboli and improved clinical results. Chest 2001;119: 25–30. Class II–III
78. Ringelstein EB, Biniek R, Weiller C, Ammeling B, Nolte PN, Thron A. Type and extent of hemispheric brain infarctions and clinical outcome in early and delayed middle cerebral artery recanalizations. Neurology 1992;42:289–298. Class II
79. Kaps M, Damian MS, Teschendorf U, Dorndorf W. Transcranial Doppler ultrasound findings in middle cerebral artery occlusion. Stroke 1990;21:532–537. Class II–III
80. Burgin WS, Malkoff M, Felberg RA, et al. Transcranial Doppler ultrasound criteria for recanalization after thrombolysis for middle cerebral artery stroke. Stroke 2000;31:1128–1132. Class II
81. Christou I, Alexandrov AV, Burgin WS, et al. Timing of recanalization after tissue plasminogen activator therapy determined by transcranial Doppler correlates with clinical recovery from ischemic stroke. Stroke 2000;31:1812–1816. Class II
82. Felberg RA, Okon NJ, El-Mitwalli A, et al. Early dramatic recovery during intravenous tissue plasminogen activator infusion: clinical pattern and outcome in acute middle cerebral artery stroke. Stroke 2002; 33:1301–1307. Class III
83. Alexandrov AV, Grotta JC. Arterial reocclusion in stroke patients treated with intravenous tissue plasminogen activator. Neurology 2002;59:862–867. Class III
84. El-Mitwalli A, Saad M, Christou I, Malkoff M, Alexandrov AV. Clinical and sonographic patterns of tandem internal carotid artery/middle cerebral artery occlusion in tissue plasminogen activator-treated patients. Stroke 2002;33:99–102. Class III
85. Labiche LA, Malkoff M, Alexandrov AV. Residual flow signals predict complete recanalization in stroke patients treated with TPA. J Neuroimag 2003;13:28–33. Class III
86. Molina CA, Montaner J, Abilleira S, et al. Time course of tissue plasminogen activator-induced recanalization in acute cardioembolic stroke: a case-control study. Stroke 2001;32:2821–2827. Class III
87. Eggers J, Koch B, Meyer K, Konig I, Seidel G. Effect of ultrasound on thrombolysis of middle cerebral artery occlusion. Ann Neurol 2003;53: 797–800.
88. Kassell NF, Torner J, Haley EC, Jane JA, Adams HP, Kongable GL. The International Cooperative Study on the Timing of Aneurysm Surgery, I. Overall management results. J Neurosurg 1990;73:18–36.
89. Grolimund P, Seiler RW. Age dependence of the flow velocity in the basal cerebral arteries—a transcranial Doppler ultrasound study. Ultrasound Med Biol 1988;14:191–198. Class III
90. Hennerici M, Rautenberg W, Schwartz A. Transcranial Doppler ultrasound for the assessment of intracranial arterial flow velocity. Part I. Examination technique and normal values. Surg Neurol 1987;27:439–448. Class II–III
91. Lysakowski C, Walder B, Costanza MC, Tramer MR. Transcranial Doppler versus angiography in patients with vasospasm due to a ruptured cerebral aneurysm: a systematic review. Stroke 2001;32:2292–2298.
92. Grosset DG, Straiton J, McDonald I, et al. Use of transcranial Doppler sonography to predict development of a delayed ischemic deficit after subarachnoid hemorrhage. J Neurosurg 1993;78:183–187. Class II
93. Kyoi K, Hashimoto H, Tokunaga H, et al. Time course of blood velocity changes and clinical symptoms related to cerebral vasospasm and prognosis after aneurysmal surgery. No Shinkei Geka 1989;17:21–30. Class II
94. Sloan MA, Burch CM, Wozniak MA, et al. Transcranial Doppler detection of vertebrobasilar vasospasm following subarachnoid hemorrhage. Stroke 1994;25:2187–2197. Class II
95. Burch CM, Wozniak MA, Sloan MA, et al. Detection of intracranial internal carotid artery and middle cerebral artery vasospasm following subarachnoid hemorrhage. J Neuroimag 1996;6:8–15. Class II
96. Wozniak MA, Sloan MA, Rothman MI, et al. Vasospasm detection by transcranial Doppler: the challenges of the anterior and posterior cerebral arteries. J Neuroimag 1996;6:87–93. Class II
97. Vora YY, Suarez–Almazor M, Steinke DE, Martin ML, Findlay JM. Role of transcranial Doppler monitoring in the diagnosis of cerebral vasospasm after subarachnoid hemorrhage. Neurosurgery 1999;44: 1237–1248. Class II
98. Sloan MA, Haley EC, Kassell NF, et al. Sensitivity and specificity of transcranial Doppler ultrasonography in the diagnosis of vasospasm following subarachnoid hemorrhage. Neurology 1989;39:1514–1518. Class II

99. Newell DW, Grady MS, Eskridge JM, Winn HR. Distribution of angiographic vasospasm after subarachnoid hemorrhage: implications for diagnosis by transcranial Doppler ultrasonography. Neurosurgery 1990;27:574–577. Class II
100. Wardlaw JM, Offin R, Teasdale GM, Teasdale EM. Is routine transcranial Doppler ultrasound useful in the management of subarachnoid hemorrhage? J Neurosurg 1998;88:272–276. Class II
101. Murayama Y, Malisch T, Guglielmi G, et al. Incidence of cerebral vasospasm after endovascular treatment of acutely ruptured aneurysms: report on 69 cases. J Neurosurg 1997;87:830–835. Class III
102. Muizelaar JP, Zweinenberg M, Rudisill NA, Hecht ST. The prophylactic use of transluminal balloon angioplasty in patients with Fisher grade 3 subarachnoid hemorrhage: a pilot study. J Neurosurg 1999;91: 51–58. Class III
103. Naidu S, Payne AJ, Moodley J, Hoffmann M, Gouws E. Randomized study assessing the effect of phenytoin and magnesium sulphate on maternal cerebral circulation in eclampsia using transcranial Doppler ultrasound. Br J Obstet Gynaecol 1996;103:111–116. Class I
104. Haley EC, Kassell NF, Torner JC, et al. A randomized controlled trial of intravenous nicardipine in subarachnoid hemorrhage: angiographic and transcranial Doppler ultrasound results. J Neurosurg 1993;78: 548–553. Class ?
105. European CGRP in Subarachnoid Haemorrhage Study Group. Effect of calcitonin-gene-related peptide in patients with delayed postoperative cerebral ischemia after aneurysmal subarachnoid haemorrhage. Lancet 1992;339:831–834. Class I
106. Findlay JM, Kassell NF, Weir BKA, et al. A randomized trial of intraoperative, intracisternal tissue plasminogen activator for the prevention of vasospasm. Neurosurgery 1995;37:168–178. Class I
107. Martin NA, Doberstein C, Zane C, Caron MJ, Thomas K, Becker DP. Posttraumatic arterial spasm: transcranial Doppler ultrasound, cerebral blood flow, and angiographic findings. J Neurosurg 1992;77:575–583. Class II
108. Chan K-H, Miller JD, Dearden NM. Intracranial blood flow velocity after head injury: relationship to severity of injury, time, neurological status and outcome. J Neurol Neurosurg Psychiatry 1992;55:787–791. Class III
109. Kakarieka A, Braakman R, Schakel EH. Clinical significance of the finding of subarachnoid blood on CT scan after head in jury. Acta Neurochir 1994;129:1–5. Class III
110. European Study Group on Nimodipine in Severe Head Injury. A multicenter trial of the efficacy of nimodipine on outcome after severe head injury. J Neurosurg 1994;80:797–804. Class I
111. Harders A, Kakarieka A, Braakman R, for the German tSAH Study Group. Traumatic subarachnoid hemorrhage and its treatment with nimodipine. J Neurosurg 1996;85:82–89. Class I
112. Lee JH, Martin NM, Alsina G, et al. Hemodynamically significant cerebral vasospasm and outcome after head injury: a prospective study. J Neurosurg 1997;87:221–233. Class III
113. Hassler W, Steinmetz H, Pirschel J. Transcranial Doppler study of intracranial circulatory arrest. J Neurosurg 1989;71:195–201. Class II
114. Hassler W, Steinmetz H, Gawlowski J. Transcranial Doppler ultrasonography in raised intracranial pressure and in intracranial circulatory arrest. J Neurosurg 1988;68:745–751. Class II
115. Zurynski Y, Dorsch N, Pearson I, Choong R. Transcranial Doppler ultrasound in brain death: experience in 140 patients. Neurol Res 1991;13:248–252. Class II
116. Petty GW, Mohr JP, Pedley TA, et al. The role of transcranial Doppler in confirming brain death. Neurology 1990;40:300–303. Class II
117. Ducrocq X, Hassler H, Moritake K, et al. Consensus opinion on diagnosis of cerebral circulatory arrest using Doppler-sonography. J Neurol Sci 1998;159:145–150.
118. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Practice parameters for determining brain death in adults. Neurology 1995;45:1012–1014.
119. Bogdahn U, Becker G, Winkler J, Greiner K, Perez J, Meurers B. Transcranial color-coded real-time sonography in adults. Stroke 1990; 21:1680–1688. Class IV
120. Eicke BM, Tegeler CH, Dalley G, Myers LG. Angle correction in transcranial Doppler sonography. J Neuroimag 1994;4:29–33. Class III
121. Bartels E, Flugel KA. Quantitative measurements of blood flow velocity in basal cerebral arteries with transcranial duplex color-flow imaging. A comparative study with conventional transcranial Doppler sonography. J Neuroimag 1994;4:77–81. Class III
122. Fujioka KA, Gates DT, Spencer MP. A comparison of transcranial color Doppler imaging and standard static pulsed wave Doppler in the assessment of intracranial hemodynamics. J Vasc Technol 1994;18: 29–35. Class III
123. Martin PJ, Evans DH, Naylor AR. Transcranial color-coded sonography of the basal cerebral circulation. Reference data from 115 volunteers. Stroke 1994;25:390–396. Class III
124. Martin PJ, Evans DH, Naylor AR. Measurement of blood flow velocity in the basal cerebral circulation: advantages of transcranial color-coded sonography over conventional transcranial Doppler. J Clin Ultrasound 1995;23:21–26. Class III
125. Becker G, Bogdahn U, Gehlberg C, Frohlich T, Hofmann E, Schlief MDR. Transcranial color-coded real-time sonography of intracranial veins. Normal values of blood flow velocities and findings in superior sagittal sinus thrombosis. J Neuroimag 1995;5:87–94. Class III
126. Hoksbergen AWJ, Legemate DA, Ubbink DT, Jacobs MJHM. Success rate of transcranial color-coded duplex ultrasonography in visualizing the basal cerebral arteries in vascular patients over 60 years of age. Stroke 1999;30:1450–1455. Class III
127. Kreja J, Mariak Z, Walecki J, et al. Transcranial color Doppler sonography of basal cerebral arteries in 182 healthy subjects: age and sex variability and normal reference values for blood flow parameters. AJR Am J Roentgenol 1999;172:213–218. Class III
128. Stolz E, Mendes I, Gerriets T, Kaps M. Assessment of intracranial collateral flow by transcranial color-coded duplex sonography using a temporal and frontal axial insonation plane. J Neuroimag 2002:12: 136–143. Class III
129. Postert T, Federlein J, Pruntek H, Buttner T. Insufficient and absent acoustic temporal bone window: potential and limitations of transcranial contrast-enhanced color-coded sonography and contrast-enhanced power-based sonography. Ultrasound Med Biol 1997;23:857–862. Class II
130. Nabavi DG, Droste DW, Schulte–Altedorneburg G, et al. Diagnostic benefit of echocontrast enhancement for the insufficient transtemporal bone window. J Neuroimag 1999;9:102–107. Class II
131. Nabavi DG, Droste DW, Kemeny V, Schulte–Altedorneburg G, Weber S, Ringelstein EB. Potential and limitations of echocontrast-enhanced ultrasonography in acute stroke patients. A pilot study. Stroke 1998; 29:949–954. Class III
132. Goertler M, Kross R, Baeumer M, et al. Diagnostic impact and prognostic relevance of early contrast-enhanced transcranial color-coded duplex sonography in acute stroke. Stroke 1998;29:955–962. Class III
133. Postert T, Braun B, Meyes S, et al. Contrast-enhanced transcranial color-coded sonography in acute hemispheric brain infarction. Stroke 1999;30:1819–1826. Class II
134. Baumgartner RW, Arnold M, Gonner R, et al. Contrast-enhanced transcranial color-coded duplex sonography in ischemic cerebrovascular disease. Stroke 1997;28:2473–2478. Class III
135. Gerriets T, Postert T, Goertler M, et al., for the DIAS (Duplex Sonography in Acute Stroke) Study Group. DIAS I: duplex–sonographic assessment of the cerebrovascular status in acute stroke. A useful tool for future stroke trials. Stroke 2000;31:2342–2345. Class II
136. Khan HG, Gailloud P, Bude RO, et al. The effect of contrast material on transcranial Doppler evaluation of normal middle cerebral artery peak systolic velocity. AJNR Am J Neuroradiol 2000;21:386–390. Class III
137. Forsberg F, Liu B, Burns PN, Merton DA, Goldberg BB. Artifacts in ultrasonic contrast agents. J Ultrasound Med 1994;13:357–365. Class III
138. Zunker P, Wilms H, Brossmann J, et al. Echo contrast-enhanced transcranial ultrasound: frequency of use, diagnostic benefit, and validity of results compared with MRA. Stroke 2002;33:2600–2603. Class III
139. Hoksbergen AWJ, Fulesdi B, Legemate DA, Csiba L. Collateral configuration of the circle of Willis. Transcranial color-coded duplex ultrasonography and comparison with postmortem anatomy. Stroke 2000; 31:1346–1351. Class II
140. Baumgartner RW, Baumgartner I, Schroth G. Diagnostic criteria for transcranial colour-coded duplex sonography evaluation of cross-flow through the circle of Willis in unilateral obstructive carotid artery disease. J Neurol 1996;243:516–521. Class II
141. Seidel G, Kaps M, Gerriets T. Potential and limitations of transcranial color-coded sonography in stroke patients. Stroke 1995;26:2061–2066. Class III
142. Gerriets T, Goertler M, Stolz E, et al., for the Duplexsonography In Acute Stroke (DIAS) study group. Feasibility and validity of transcranial duplex sonography in patients with acute stroke. J Neurol Neurosurg Psychiatry 2002;73:17–20.
143. Maurer M, Shambal S, Berg D, et al. Differentiation between intracerebral hemorrhage and ischemic stroke by transcranial color-coded duplex-sonography. Stroke 1998;29:2563–2567. Class III
144. Becker G, Greiner K, Kaune B, et al. Diagnosis and monitoring of subarachnoid hemorrhage by transcranial color-coded real-time sonography. Neurosurgery 1991;28:814–820. Class III–IV
145. Baumgartner RW, Mattle HP, Kothbauer K, Schroth G. Transcranial color-coded duplex sonography in cerebral aneurysms. Stroke 1994;25: 2429–2434. Class II–III
146. Wardlaw JM, Cannon JC. Color transcranial "power" Doppler ultrasound of intracranial aneurysms. J Neurosurg 1996;84:459–461. Class II
147. Griewing B, Motsch L, Piek J, Schminke U, Brassel F, Kessler C. Transcranial power mode Doppler duplex sonography of intracranial aneurysms. J Neuroimag 1998;8:155–158. Class II
148. Proust F, Callonec F, Clavier E, et al. Usefulness of transcranial color-coded sonography in the diagnosis of cerebral vasospasm. Stroke 1999;30:1091–1098. Class II
149. Seidel G, Kaps M, Dorndorf W. Transcranial color-coded duplex sonography of intracerebral hematomas in adults. Stroke 1993;24:1519–1527. Class II

Assessment: Transcranial Doppler ultrasonography: [RETIRED]: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology*

M. A. Sloan, A. V. Alexandrov, C. H. Tegeler, et al.

Neurology 2004;62;1468-1481
DOI 10.1212/WNL.62.9.1468