demchuk!

VU Scientific Articles

The Journal for Vascular Ultrasound 39(4):183–187, 2015

Transcranial Doppler: Uses in Stroke Prevention

J. David Spence, MD, FRCPC, FAHA

ABSTRACT Transcranial Doppler (TCD) is useful in stroke prevention for at least three purposes: diagnosis of intracranial stenosis, detection of right-to-left shunt in patients with suspected paradoxical embolism, and detection of microemboli in patients with carotid stenosis. Other uses may include assessment of cerebral blood flow, which is not discussed in this review. TCD saline studies are more sensitive than transesophageal echocardiography, and more strongly predictive of risk of recurrent events. TCD embolus detection is the best-validated method for identifying among patients with asymptomatic carotid stenosis the few who could benefit from carotid endarterectomy or stenting.

Diagnosis of Intracranial Stenosis

The SAMPPRIS trial[1] showed clearly that patients with intracranial stenosis benefit more from intensive medical therapy than from stenting. Patients randomized to stenting had nearly three times the risk of stroke or death within 30 days (14.7% versus 5.8%; $p = 0.002$). Nevertheless, it is useful to diagnose intracranial stenosis, because more intensive medical therapy is needed, including dual antiplatelet therapy.

Intracranial stenosis is more common in Asian patients and patients with diabetics; Lam et al.[2] found that it was present in a third of patients with asymptomatic carotid stenosis. This was more common among patients with diabetics (45% versus 29%; $p = 0.017$). Among patients with asymptomatic carotid stenosis, the presence of intracranial stenosis significantly increased the risk of stroke/death/transient ischemic attack (TIA) (18% of patients with intracranial stenosis versus 10% with no stenosis; $p = 0.042$).[2]

Intracranial stenosis of 50% or greater of a middle cerebral artery (MCA) is diagnosed by a mean systolic velocity of 100 cm/s in the absence of a generalized hyperdynamic state (Figure 1). This criterion was validated against angiography in 2002 by Felberg et al.[3] for the detection of MCA stenosis with transcranial Doppler (TCD), and in 2011 by Zhao et al.[4]

Microembolus Detection for Identification of High-Risk Asymptomatic Carotid Stenosis

Microemboli in the MCA distal to a carotid stenosis can be detected with TCD. A helmet holds TCD probes in place, the MCAs are Insonated through the thinnest part of the temporal bone at a depth of ≈4 cm, and the M-mode and Doppler channels are monitored for the occurrence of microemboli. Microembolic signals are defined by unidirectionality, duration of shorter than 300 ms, and intensity of more than 8 dB above the Doppler background, with adjustment of gain to enhance detection. International consensus recommendation specify settings for microembolus detection as follows: leading cols of 255 mm, trailing cols of 255 mm, a microemboli threshold of 9 mm, and rejection of 55 mm.[5] Figure 2 shows a microembolus.

Most patients (90%) with asymptomatic carotid stenosis would be better treated with intensive medical therapy than with stenting or endarterectomy. This was shown in 2005 by Spence et al.[6] in a study of TCD embolus detection, in 319 patients with asymptomatic carotid stenosis: the 1-year risk of stroke was only 1% among the 90% of patients with no microemboli, versus 15.6% among those with two or more microemboli in 1 h of monitoring. This was validated in 2010 by the Asymptomatic Carotid Embolus Study[7] in 467 patients. Using repeated TCD studies at 6, 12, and 18 months, and a single microembolus as a positive test, the authors found microemboli in 16.4% of patients. They found that the annual risk of ipsilateral stroke was 3.62% in patients with embolic signals and 0.70% with none. A smaller study by Abbott et al. (202 patients) and repeated TCD recordings, with single microemboli regarded as positive, showed a trend to higher risk with microemboli. In the 2005 report, Spence et al.[6] noted that microemboli became less frequent with medical therapy: among those with microemboli at baseline, microemboli were found in only 34% at a 1-year follow-up, and only 9% at a 2-year follow-up. Among patients with no microemboli at baseline, microemboli were found in only 1.4% at a 1-year follow-up, and only 1% at the 2-year follow-up.

From Stroke Prevention and Atherosclerosis Research Centre, Robarts Research Institute, Western University, London, Ontario, Canada.

Accreditation Statement: This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the University of Cincinnati and the Society for Vascular Ultrasound. The University of Cincinnati is accredited by the ACCME to provide continuing medical education for physicians. The University of Cincinnati designates this journal activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credits commensurate with the extent of their participation in the activity.

Address correspondence to: J. David Spence, MD, FRCPC, FAHA, Stroke Prevention and Atherosclerosis Research Centre, Robarts Research Institute, Western University, 1400 Western Road, London, ON Canada N6G 2V4. E-mail: dspence@robarts.ca

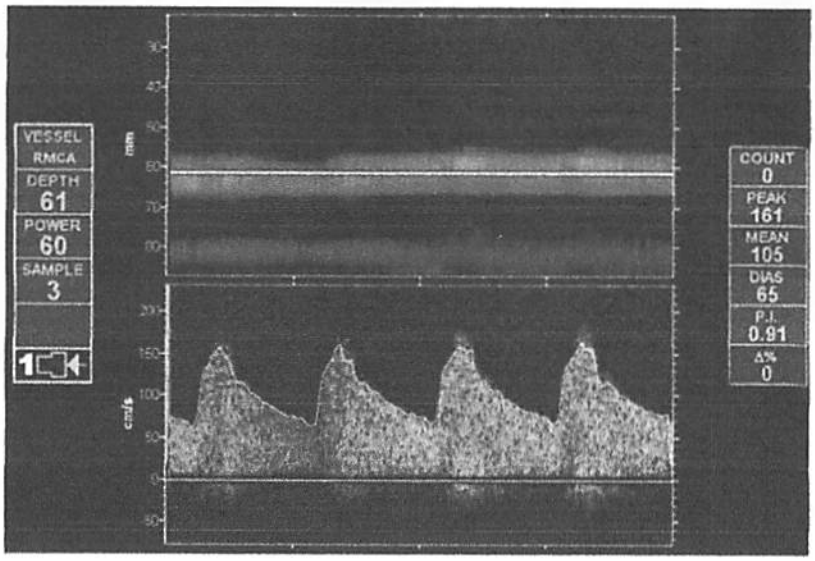

Figure 1

Intracranial stenosis. The peak velocity of 160, with a mean velocity of 105 cm/s, suggests stenosis of the middle cerebral artery.

In 2010, Spence et al. reported[8] on the effects of more intensive medical therapy based on measurement of carotid plaque burden,[9] in patients with asymptomatic carotid stenosis. Among 468 patients, they compared results in 199 patients enrolled before 2003, when "treating arteries" was implemented in their clinic, versus 269 patients enrolled after 2003. The prevalence of microemboli dropped from 12.6% to 3.7% (Figure 3) and more importantly, the rate of events declined by more than 80%: the 2-year risk of stroke dropped from 8.8% to 1%, and the 2-year risk of myocardial infarction from 7.6% to 1%. Despite these major improvements with intensive medical therapy, the risk of stroke/death/TIA remained higher among patients with microemboli who were enrolled after 2003 (Figure 4).

It is curious that TCD is not more widely used to identify high-risk asymptomatic carotid stenosis. Most patients with asymptomatic stenosis (90%) would be

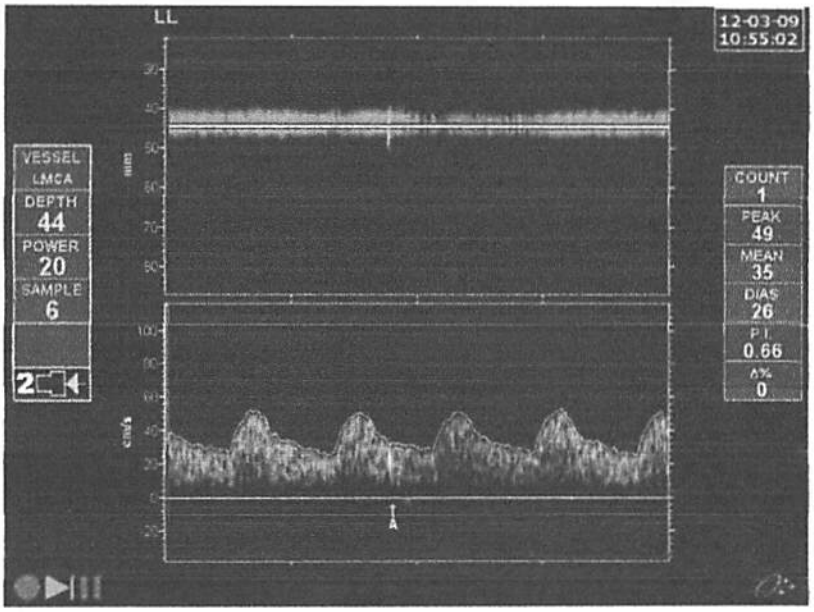

Figure 2

Microembolus in a patient with asymptomatic carotid stenosis. The upper channel is an M-mode image of an embolus in the middle cerebral artery; the lower panel shows the high-intensity transit signal in the Doppler channel. Besides the visual appearance of the microembolus, a characteristic clicking sound is heard.

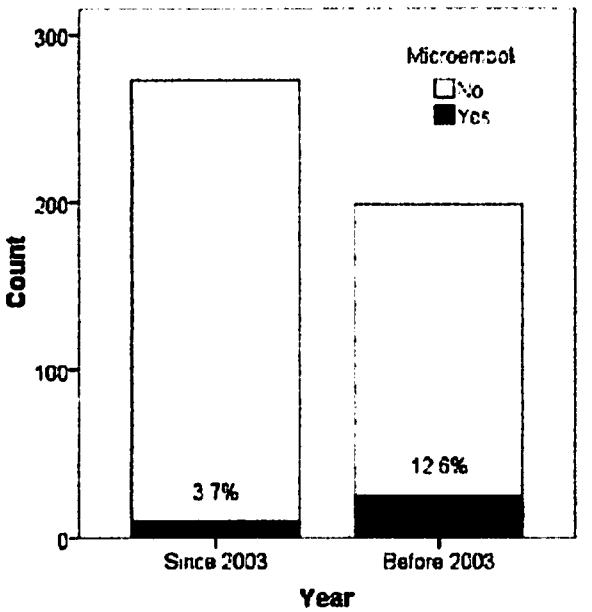

Figure 3

Decline of microemboli in patients with asymptomatic carotid stenosis. After implementation in 2003 of a program of more intensive medical therapy based on measurement of carotid plaque burden, the prevalence of microemboli dropped from 12.6% to 3.7%.

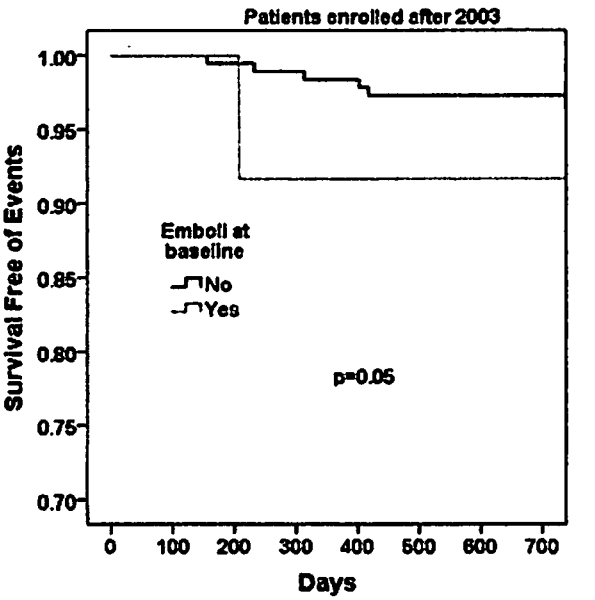

Figure 4

Risk of stroke, TIA, or death with microemboli. Even after implementation of more intensive medical therapy in 2003, the presence of microemboli predicted survival free of stroke, TIA, or death in Kaplan–Meier analysis.

better off with intensive medical therapy, so doing carotid endarterectomy or stenting is more likely to harm than help them.[10] The cost of a TCD machine is about the same as the reimbursement for two carotid stenting procedures, and persons familiar with ultrasound can accomplish training and certification in a 2-day course. Although there are other approaches to identifying high-risk asymptomatic stenosis,[10] they are more costly, and some involve radiation.

TCD Saline Studies for Diagnosis of Right-to-Left Shunt

Several types of stroke occur when material proceeding via the venous circulation to the heart passes from the right side of the heart to the left side without being filtered by the pulmonary circulation. They include fat embolism, air embolism, amniotic fluid embolism, and paradoxical embolism in patients with thrombi that embolize from a vein (usually in the setting of deep vein thrombosis, but a large venous thrombus is not a necessary precondition).

Paradoxical embolism accounts for 4%[11] to 5.5%[12] of first strokes, but a higher proportion among patients with no apparent cause such as hypertension, dissection, vasculitis, large artery disease, or a known cardioembolic source (cryptogenic stroke). In patients with cryptogenic stroke, there are many important clinical clues to paradoxical embolism.[12] Because a paradoxical embolus coincides with a pulmonary embolus, clinical clues include tachycardia, hypoxemia, and dyspnoea at the onset of stroke. Other clues include causes of increased right-sided pressure (a Valsalva maneuver preceding the stroke, and sleep apnea), and probably because sleep apnea increases right-sided pressure, waking up with stroke. Factors that predispose to formation of venous thrombi include coagulation disorders (the commonest of which is an elevated homocysteine level (often due to missed metabolic deficiency of vitamin B_{12}), prolonged sitting, such as a long plane ride or car ride, previous history of deep vein thrombosis, pulmonary embolism, deep vein thrombosis, and the presence of signs of venous insufficiency (a patch of hemosiderin deposition in the skin of the medial side of the foot, just below the ankle).

Right-to-left shunting (RLS) can occur in patients with atrial septal defect, ventricular septal defect, pulmonary arteriovenous fistula, and most commonly, patent foramen ovale (PFO). A difficulty in diagnosing paradoxical embolism is that PFO is very common, ≈25% of the population. This means that among patients with stroke and a PFO, the PFO will be incidental in ≈80% of patients. This probably accounts for the failure to show benefit in studies of percutaneous closure of PFO.

An RLS can be diagnosed by echocardiography, with contrast material or saline bubbles seen to pass from the right atrium to the left atrium. Transesophageal echocardiography (TEE) is more sensitive than transthoracic echo.[13] TCD saline studies (bubble studies) have been validated as an alternative to TEE,[14] and indeed there is some evidence, discussed below, that TCD bubble studies are more sensitive and more strongly predictive of recurrent stroke than TEE.[15,16]

TCD Bubble Study

In our lab we use a Spencer Technologies ST3 Power M-mode TCD (Spencer Techologies, Redmond WA),

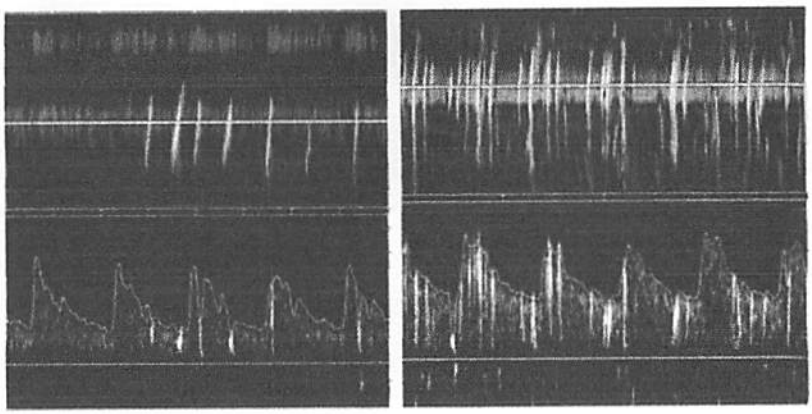

Figure 5

Transcranial Doppler bubble study. The left panel shows a Spencer grade II right-to-left shunt; the right shows a grade IV shunt.

with bitemporal 2-MHz probes. First, patients are assessed for the presence of temporal windows on both sides. If ultrasound access to at least one MCA is confirmed, a head frame is placed on the head to hold the two TCD probes in place for monitoring; insonation is focused at a depth of 40–60 mm.

Patients are placed in a semi-recumbent position and a 21-gauge butterfly needle is inserted in an antecubital vein of the most convenient forearm. The catheter of the butterfly needle is connected with a three-way stopcock system to two syringes. One contains 8 mL of saline solution and 1 mL of the patient's blood (to stabilize the bubbles)[17]; the second contains 1 mL of room air. The saline solution, blood, and air are mixed at least 10 times to form the microbubbles. Microbubbles are usually injected twice; first during normal respiration, and then after a strenuous Valsalva maneuver, beginning ≈5 seconds after the injection of the microbubbles and maintained for at least seconds. A drop in MCA blood velocity can assess the adequacy of the Valsalva maneuver. Embolic tracks are counted over a 60-s post-injection interval. Early appearance of bubbles (within several cardiac cycles) indicates a cardiac pathway for shunting; patients with only late bubbles usually will have a pulmonary arteriovenous fistula.

Spencer's logarithmic grading system[18,19] is used to assess the severity of RLS, based on the following criteria: grade 0: no microemboli detected; grade I: 1–10 microemboli; grade II: 11–30 microemboli; grade III: 31–100 microemboli; grade IV: 101–300 microemboli; grade V: >300 microemboli. Figure 5 shows examples of a grade II and a grade V shunt. A second injection following Valsalva maneuver is not necessary in patients with a large shunt during normal respiration.

Tobe et al.[20] reported that among 284 patients with suspected paradoxical embolism in whom an RLS was demonstrated, TEE failed to show an RLS in 43 (15.4%) of the patients; surprisingly, this occurred even in some patients with high-grade shunts (Spencer grade) on TCD. Among patients with a negative echo, TCD Spencer grades were I in 45.5%, II in 32.2%, III in 13.3%, IV in 7.1%, and V in 4.7%. Kaplan–Meier survival free of stroke or TIA was predicted significantly by TCD shunt grade of III or more ($p = 0.028$), but not by RLS on echo ($p = 0.42$) or by anatomical features such as atrial septal aneurysm and septal mobility. Several other studies found that echocardiographic features did not predict risk of stroke.[21–23] Others have also reported that TCD was more sensitive than TEE for detection of RLS.[23,24] One likely reason is that sedation for TEE may prevent an adequate Valsalva maneuver.[25]

There are some problems to be kept in mind when interpreting TCD bubble studies. One is that occasionally a bubble study may be falsely negative, if the PFO is occluded by thrombus.[26] Thus, if suspicion is strong, a repeat TCD bubble study may be warranted. A second is that there may be small inducible arteriovenous anastomoses[27] that can result in the passage of several small bubbles, so the appearance of three or four late bubbles should be regarded as a negative test.

Conclusion

TCD is useful for diagnosis of intracranial stenosis, for identification of high-risk patients with asymptomatic carotid stenosis, and for assessment of suspected paradoxical embolism. TCD should be available at all stroke centers. Patients with asymptomatic carotid stenosis should probably not be subjected to endarterectomy or stenting without TCD embolus detection, and percutaneous closure of a PFO should probably not be performed unless a TCD bubble study shows a substantial shunt.

Acknowledgments

Much of J.D.S.'s work with TCD was supported by grants from the Heart and Stroke Foundation of Canada. J.D.S. has no conflict of interest in relation to manufacturers of TCD equipment.

References

1. Chimowitz MI, Lynn MJ, Derdeyn CP, et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. *N Engl J Med* 2011;365:993–1003.

2. Lam TD, Lammers S, Munoz C, et al. Diabetes, intracranial stenosis and microemboli in asymptomatic carotid stenosis. *Can J Neurol Sci* 2013;40:177–181.