Review Article/Brief Review

Transcranial Doppler monitoring in subarachnoid hemorrhage: a critical tool in critical care

[Monitorage par Doppler transcrânien lors d'une hémorragie sous-arachnoïdienne : un outil indispensable aux soins intensifs]

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Purpose: To review the literature regarding the use of transcranial Doppler ultrasonography (TCD) for monitoring cerebral vasospasm following subarachnoid hemorrhage (SAH).

Source: We searched Medline (1980 to August 2007) and Embase (1980 to August 2007) and reviewed all relevant manuscripts regarding TCD and SAH.

Principal findings: Currently, the gold standard for vasospasm diagnosis is cerebral angiography, replaceable by computed tomography angiography, only when angiography is not available. Obviously, it is not feasible to perform such investigation as frequently as bedside clinical assessment. Repeated clinical assessments of a patient's neurological status carry the problem of detecting the clinical signs and symptoms of vasospasm, which occur only after vasospasm has already manifested its deleterious effects on the cerebral parenchyma. Transcranial Doppler ultrasonography is a relatively new, non-invasive tool, allowing for bedside monitoring to determine flow velocities indicative of changes in vascular calibre. Transcranial Doppler ultrasonography can be useful pre-, intra- and post-operatively, while helping to recognize the development of cerebral vasospasm before the onset of its clinical effects.

Conclusion: Vasospasm following SAH is a very important source of morbidity and mortality. Too often, the first sign is a neurologic deficit, which may be too late to reverse. Transcranial Doppler ultrasonography assists in the clinical decision-making regarding further diagnostic evaluation and therapeutic interventions. When performed in isolation, the contribution of TCD to improving patient outcome has not been established. Nevertheless, TCD has become a regularly employed tool in neurocritical care and perioperative settings.

***Objectif** : Passer en revue la littérature concernant l'utilisation de l'échographie Doppler transcrânienne (TCD) pour surveiller un vasospasme cérébral survenu à la suite d'une hémorragie sous-arachnoïdienne (SAH).*

***Source** : Nous avons effectué des recherches sur Medline (1980 à août 2007) et Embase (1980 à août 2007) et révisé tous les manuscrits pertinents concernant la TCD et la SAH.*

***Constatations principales** : À l'heure actuelle, l'angiographie est l'étalon or pour diagnostiquer un vasospasme. Celle-ci peut être remplacée par l'angiographie par tomodensitométrie seulement lorsqu'une angiographie n'est pas disponible. Il est évident qu'il n'est pas possible d'effectuer de telles recherches aussi fréquemment que les évaluations cliniques au chevet du malade. Des évaluations cliniques répétées de l'état neurologique d'un patient donné ont pour objectif primaire la détection des signes et symptômes cliniques du vasospasme, lesquels ne surviennent qu'après que le vasospasme a manifesté ses effets nuisibles sur le parenchyme cérébral. L'échographie Doppler transcrânienne est un outil relativement nouveau et non invasif qui permet un monitorage au chevet du patient afin de déterminer les vitesses du débit qui indiquent les changements dans le calibre vasculaire. L'échographie Doppler transcrânienne peut être utile avant, pendant et après l'opération tout en constituant un outil précieux pour identifier le développement d'un vasospasme cérébral avant que ses effets cliniques ne se manifestent.*

***Conclusion** : Le vasospasme à la suite d'une SAH est une cause majeure de morbidité et de mortalité. Trop souvent, le premier signe visible d'un vasospasme est un déficit neurologique, et il pourrait être trop tard déjà pour qu'il soit réversible. L'échographie Doppler transcrânienne est un outil qui assiste la prise de décision clinique concernant une évaluation diagnostique approfondie et des interventions thérapeutiques. Il n'a pas été démontré que la TCD,*

CAN J ANESTH 2008 / 55: 2 / pp 112–123

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Disclosure: No funding sources were supplied. There are no conflicts of interest.

Accepted for publication May 24, 2007.

Revision accepted November 19, 2007.

utilisée seule, améliore le suivi des patients. Cependant, la TCD est devenue un outil régulièrement employé dans des contextes de soins intensifs neurologiques et périopératoires.

CEREBRAL vasospasm is the delayed narrowing of large capacitance arteries at the base of the brain following subarachnoid hemorrhage (SAH), often associated with radiographic or clinical evidence of diminished perfusion in the distal territory of the affected arteries. Cerebral vasospasm contributes to high levels of morbidity and mortality. It may evolve anywhere between the third and the seventh day following the initial hemorrhage in the neural parenchyma.[1] A typical course for vasospasm is for it to increase on the fourth day after SAH, with a declining trend following the 14th day.[2] This phenomenon is primarily located adjacent to the initial hemorrhage, or it can be multifocal affecting all areas of the brain. Although the mechanism of vasospasm is not well understood, the hypothesis is that extravasated blood from the initial hemorrhage triggers secondary cellular mechanisms. This manifests clinically as decreased cerebral blood flow caused by arterial vasoconstriction, and the patient exhibits evidence of delayed neurological deficit. Several laboratories have elucidated potential secondary mechanisms of arterial vasospasm, and postulated mechanisms that include damage to endothelial cells (reducing nitric oxide production) with corresponding increased nitric oxide metabolites in the cerebrospinal fluid, and the degradation of contractile and cytoskeletal proteins due to increased concentrations of intracellular calcium.[3–5] These complex and multifaceted mechanisms culminate in vascular smooth muscle contraction.

Incidence of vasospasm

Occasionally there is confusion over the word "vasospasm". The term "vasospasm" refers to the phenomenon of narrowing of arteries seen after SAH. "Symptomatic vasospasm" and "delayed ischemic deficit" are considered as synonymous, referring to the clinical syndrome wherein the narrowing of the arteries is severe enough to cause ischemic symptoms. "Angiographic vasospasm" refers to the estimation of arterial narrowing by means of a cerebral angiography. Delayed ischemic deficit associated with symptomatic vasospasm usually appears shortly after the onset of angiographic vasospasm, with the acute or sub-acute development of focal or generalized symptoms and signs.[6,7]

Symptomatic vasospasm occurs in 20–30% of patients affected by SAH and leads to a 15–20% risk of stroke or death.[8] Indeed, progression to cerebral infarction occurs in approximately 50% of symptomatic cases; recovery without deficit in the remaining individuals may occur despite the persistence of angiographic vasospasm.[6]

A review by Dorsch and King reported that the incidence of angiographic vasospasm ranges between 40 and 97% of affected individuals, with an average of 67.3%. Their review of 38 angiographic studies, including 2,738 cases, found the highest incidence of vasospasm occurred between the tenth and the 17th day post-event, with a peak at day 13. Approximately 10% of SAH patients will be permanently debilitated and another 10% will die because of the secondary vasospasm. The authors also believed that the higher incidences were more accurate and, if daily angiography were performed, the true incidence of angiographic vasospasm would be closer to 100%.

Management of vasospasm

The primary SAH, and a number of secondary insults in the post-hemorrhagic period, may equally affect the clinical outcome. While the effects of the primary insult are not modifiable, secondary insults, including vasospasm, are potentially preventable, or at least attenuated. Current prophylactic and therapeutic treatments of vasospasm include early aneurysm closure, removal of cisternal blood, triple-H therapy (hypervolemia, hemodilution, and hypertension), balloon angioplasty, and nimodipine (a dihydropyridine calcium antagonist).[9] It must be noted that triple-H therapy is not completely safe, and its prophylactic use in patients with SAH, without proven vasospasm, should be applied with utmost caution. Indeed, triple-H therapy may cause further damage and result in cerebral or pulmonary edema, renewed bleeding in unsecured aneurysms, hemorrhagic transformation in areas of infarction, congestive heart failure, and myocardial infarction. [10,11] The same risks are obviously present, even when triple-H therapy is given to patients with proven vasospasm and delayed ischemic deficit.[12] A recent animal research and clinical intervention study investigated the effect of the three components of the triple-H therapy.[13] This study showed that vasopressor-induced hypertension caused a significant increase in regional cerebral blood flow and brain tissue oxygenation ($P_{Br}O_2$) in ten patients with subarachnoid hemorrhage. Interestingly, this study also showed that, while volume expansion resulted in an increase in cerebral perfusion, hypervolemia reversed the hypertension-induced increase on $P_{Br}O_2$.

A recent systematic review showed that, despite the widespread use of triple-H therapy to prevent vasospasm after SAH, there is insufficient evidence-based data to make recommendations for its use as a prophylactic treatment for vasospasm.[14]

Here we focus on vasospasm; but subarachnoid hemorrhage can involve a number of secondary complications other than vasospasm, including increased intracranial pressure, hydrocephalus, re-bleeding, ischemia, and seizures. These interconnected disease processes make it difficult to differentiate the exact cause of the delayed neurological deficits observed clinically.

Detection of delayed ischemic deficit

Assessment of level of consciousness and focal deficits provide a concise and practical method for predicting the probability of a poor outcome after SAH.[15] However, clinical signs of neurological deterioration, detected during repeated assessments, have less utility in prophylactic treatment. Such signs are evident only after the occurrence of an acute event and are potentially not detectable due to coma, sedation, or neuromuscular blockade.[16] A recent review by White[17] evaluates the evidence for the use of transcranial Doppler ultrasonography (TCD) in the critical care population and describes its potential usefulness in a number of different conditions.

The aim of this review is to focus on manuscripts evaluating the use of TCD for monitoring vasospasm, post-SAH, and to describe the improvements that the use of colour- coded sonography brings to transcranial Doppler monitoring. This relatively new diagnostic technique appears to be an effective bedside tool for monitoring the trend of cerebral flow velocity (index of vasospasm), allowing patients to be cared for more appropriately, before the onset of new neurological deficits. We begin by very briefly describing the multimodal and emerging techniques utilized to monitor the onset and the progression of vasospasm following SAH.

Search strategy

We searched Medline (1980 to August 2007) and Embase (1980 to August 2007) databases. We reviewed all relevant manuscripts relating to transcranial Doppler and subarachnoid hemorrhage using the following strategies:

Medline (Ovid)

1) Subarachnoid Hemorrhage; 2) Intracranial Aneurysm/; 3) Rupture, Spontaneous/; 4) 2 and 3; 5) exp brain/; 6) Aneurysm, Ruptured/; 7) 5 and 6; 8) Vasospasm, Intracranial/; 9) sah.tw.; 10) Intracranial hemorrhages/ or cerebral hemorrhages/ or Vasospasm, Intracranial/; 11) 1 or 4 or 7 or 8 or 9 or 10; 12) Ultrasonography, Doppler, Transcranial/ 13) ultrasonography, Doppler, color/ or ultrasonography, Doppler, duplex/; 14) exp ultrasonography/; 15) Ultrasonography, Doppler/; 16) tcd.tw.; 17) 12 or 13 or 14 or 15 or 16; 18) 11 and 17.

Embase (Ovid)

1) Subarachnoid hemorrhage/; 2) Intracranial aneurysm/; 3) Rupture/; 4) 2 and 3; 5) Aneurysm rupture/; 6) exp brain/; 7) 5 and 6; 8) Brain vasospasm/; 9) sah.tw.; 10) intracranial hemorrhages/ or cerebral hemorrhages/ or vasospasm, intracranial/; 11) Brain artery aneurysm rupture/; 12) 1 or 4 or 7 or 8 or 9 or 10 or 11; 13) Doppler echography/; 14) echoencephalography/; 15) color ultrasound flowmetry/; 16) tcd.tw.; 17) 12 and 16.

Monitoring SAH vasospasm in intensive care unit: emerging diagnostic tools

The first description of transcranial Doppler recordings of intracranial arteries was published in 1982.[18] Two years later, the same authors suggested the use of TCD for the diagnosis and monitoring of cerebral vasospasm.[19] Since then, an increasing number of manuscripts on the use of TCD for monitoring vasospasm have been published. The major advantages of TCD are as follows: it is non-invasive; it allows for bedside monitoring; dye contrast agents are not used; and it is less expensive overall compared to other techniques.

Intra-arterial digital subtraction angiography, also known as cerebral angiography, is currently the reference-standard for the diagnosis of cerebral vasospasm. It is an expensive and invasive procedure, which does not allow for bedside monitoring, making it difficult to apply regularly in critically ill patients. Moreover, cerebral angiography carries the risks of arterial dissection, renal injury, and stroke.[20,21] Computed tomography (including computed tomography angiography (CTA) and single photon emission computed tomography) and magnetic resonance angiography have been utilized successfully for detecting vasospasm. Unfortunately, considered alone, these techniques have limited sensitivity in detecting distal vasospasm.[22–24] In a prospective study, Anderson and colleagues[25] demonstrated that CTA is highly sensitive and specific in detecting no spasm or severe vasospasm in proximal arteries. It is less accurate for detecting mild and moderate vasospasm in distal arteries. Digital subtraction angiography offers the advantage of a prompt

treatment (balloon angioplasty), whereas CTA could potentially delay treatment.

In addition to TCD, cerebral angiography, and CTA, a variety of new techniques are emerging. These techniques have the potential to detect SAH-induced vasospasm earlier in the course of the disease.

Continuous electroencephalography is a non-invasive bedside technique that correlates well with the cerebral topography and allows clinicians to monitor cerebral metabolism, seizure activity, and focal ischemia of the brain.[16,26] Using continuous electroencephalography offers a new approach for effectively monitoring vasospasm. Classen *et al.* used quantitative, continuous electroencephalography to associate decreases in alpha power/delta power ratios with delayed cerebral ischemia in patients with low grade SAH.[27] They suggest that this decrease of the alpha power/delta power ratios can lead to detection of vasospasm earlier than with TCD, allowing a prompt therapeutic intervention.[27,28] Moreover, a study by Vespa *et al.*[29] showed that a two-grade decrease in relative alpha variability preceded documented angiographic vasospasm and increased with resolution of the vasospasm. However, this technique has yet to be fully validated, and problems with analysis and dependence on trained neurophysiologists to properly interpret the data, preclude its widespread implementation.[16,27,29]

Research in monitoring of brain tissue oxygen, carbon dioxide partial pressure, and pH has yielded some potentially useful tools in monitoring vasospasm following SAH. A study by Charbel *et al.*[30] demonstrated that patients who had vasospasm following SAH displayed increases in carbon dioxide pressure (pCO_2) and decreases in pH when compared to controls. Although interesting, this study is limited by the sample size (ten patients with SAH, three of whom had vasospasm). Moreover, the authors did not detail the patients' neurological status and they did not comment on whether they observed an arterial pCO_2 difference between the two groups. Animal experiments performed by Jabre *et al.*[31] demonstrated that occlusion of the carotid arteries (creating an ischemic environment) resulted in a decrease in pH, as measured with the portable Khuri monitor. This research data, although not yet clinically applicable, may lead to the development of useful tools for the early recognition of vasospasm.

Transcranial cerebral oximetry, also named near infrared spectroscopy (NIRS), is a non-invasive technology that measures hemoglobin oxygen saturation in the human brain. Transcranial cerebral oximetry may detect the effect of vasospasm through the measurement of impaired oxygen delivery, as NIRS mainly measures oxygen venous saturation.[32] The utility of NIRS alone in monitoring vasospasm is very limited, since its clinical reliability, sensitivity, and specificity for detecting brain ischemia has not yet been established. However, Ekelund *et al.*,[32] in an observational study of 14 patients with SAH, showed the correlation between NIRS and TCD, and concluded that NIRS may enhance the TCD's reliability in detecting cerebral vasospasm following SAH, thus giving clinicians a better understanding of changes in cerebral blood flow during vasospasm.

Biochemical markers in the cerebrospinal fluid have the potential to help in the early prediction of vasospasm and the severity of SAH. S-100 is a cerebrospinal fluid protein marker of axonal and neuronal degeneration; and its concentrations have been related to the severity of SAH and the outcome of the patient's delayed neurological deficits. It appears that this marker will potentially help to predict which patients will experience progressive vasospasm.[16]

Transcranial Doppler ultrasonography

Principles of TCD

First used by Aaslid and colleagues[18] in 1982, transcranial Doppler ultrasonography has evolved into an effective bedside tool to follow the progression of vasospasm. It is a non-invasive technique, which monitors blood flow velocity (FV) in the basal cerebral arteries and provides useful information about cerebral hemodynamics. Transcranial Doppler ultrasonography is based on the hemodynamic principle that the velocity of blood flow in a given artery is inversely related to the cross-sectional area of that artery. The TCD probe emits an ultrasonic beam at a given frequency f_0 and speed c. This ultrasonic beam crosses the skull at points called "acoustic windows", and it is reflected back from the moving red blood cells at an altered frequency f_e. The difference in frequency between the transmitted wave and the received wave is called the "Doppler shift" or "Doppler effect", and can be calculated as:

$$f_d = f_e - f_0.$$

The velocity v of the moving red blood cells can be calculated as:

$$V = c \times f_d / 2 \times f_0 \times \cos\theta$$

Where θ is the angle between the direction of the ultrasonic beam and the direction of blood flow.

Transcranial Doppler uses low frequency (2 MHz), focused, pulsed wave probes to insonate the major cerebral vessels. Transcranial Doppler ultrasound is

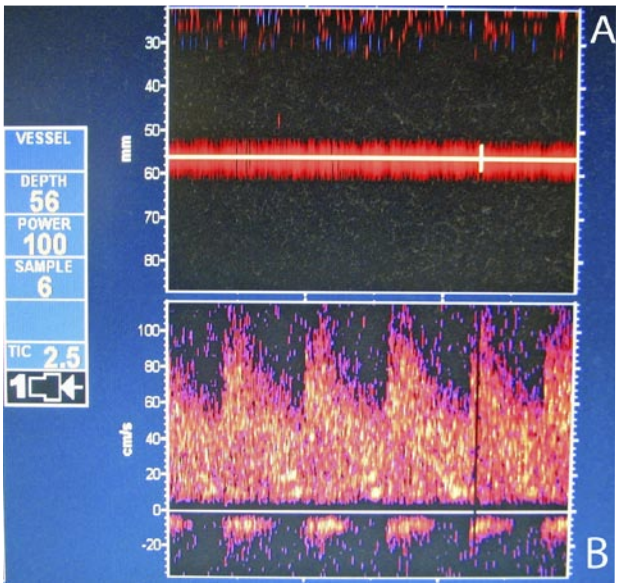

FIGURE 1 Middle cerebral transcranial Doppler ultrasonography, as seen on M-mode transcranial Doppler machine screen. A) The top of the screen shows the power M-mode Doppler signal. The sampling depth is 56 mm. B) Pulsed wave Doppler. Systolic, diastolic, and time-averaged mean values are calculated from the flow velocity waveform.

pulsed and the time interval from pulse emission to pulse reception can be manipulated. The time interval determines the depth from which any Doppler frequency shift is detected. Since erythrocytes move at different speeds, the Doppler signal is a mixture of different frequency components displayed as a graph of a full range of velocities at a particular point of a vessel. Therefore, with the use of spectral analysis, three-dimensional Doppler data are presented in a two-dimensional format (time on the horizontal axis and velocity on the vertical axis). The brightness of the signal on the screen represents the TCD signal intensity (Figure 1). Systolic, diastolic, and time-averaged mean values are then calculated from the FV waveform. Since the pulsed wave TCD concentrates the energy in the wave emission phase and spares energy during the interval phase, the pulsed-wave beam has greater strength per wave-unit. The introduction of colour TCD has further improved this technique by giving colour-coding flow information to denote the directionality of the blood flow (Figure 1). This technology is called power M-mode TCD.

If properly performed, power M-mode TCD can yield very accurate results on vascular flow velocities, but it is heavily operator-dependent.[33] Accuracy is subject to a variety of factors, including the angle between the direction of flow and the sound beam, the insonating frequency, and the velocity of the moving blood. Power M-mode TCD allows the measurement of velocity, direction, and depth of the flow signal. When performing TCD recordings, it is essential to use the same probe, transducer, and frequency at the same position and angle of insonation. Unfortunately, it is difficult to ensure that images are taken at the same position and with the same angle of insonation, when repeating TCD recordings on a daily basis, and, in particular, when different operators are involved. Furthermore, while it is usually possible to find the anterior, middle, and posterior cerebral arteries through the temporal window,[34] their overlapping range of depth renders it difficult to distinguish between them (Table I). Nevertheless, due to the relatively low cost of the machine, Power M-mode TCD is the most commonly used technique utilized to detect vasospasm at the bedside (Figure 2).

TABLE I Probe direction, depth, and flow direction of cerebral arteries in patients with normal Circle of Willis anatomy

	Probe direction	*Depth (mm)*	*Flow direction*
ACA	Anterior	60-75	Away
MCA	90°	40-65	Toward
PCA	Posterior	55-70	Toward

ACA = anterior cerebral artery; MCA = middle cerebral artery; PCA = posterior cerebral artery.

Transcranial colour-coded duplex sonography (TCCS) has further improved this technique by giving a dimensional representation of the basal arteries, in addition to the colour-coding flow information over a grey image to denote the directionality of the blood flow. Transcranial colour-coded duplex sonography improves on pulsed wave TCD by allowing an operator to outline the brain parenchyma and the intracranial bony structure, and to illustrate the whole course of the main cerebral arteries (Figure 3), allowing precise measurement of the flow parameters. Transcranial colour-coded duplex sonography makes the measurement of angle of correction for flow velocities feasible by more clearly delineating the basal cerebral arteries, thus improving consistency and accuracy of transcranial ultrasound. Indeed, the angle of insonation can cause large errors when flow velocities are measured without the angle correction.[35] Moreover, TCCS provides a two-dimensional representation of the basal arteries, making the single investigation more repro-

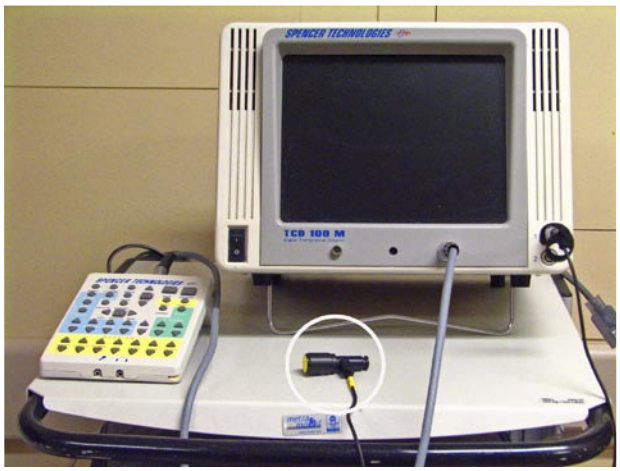

FIGURE 2 M-mode transcranial Doppler machine. Transcranial Doppler probe is shown in the white circle. (Property of Trauma Neuro Critical Care Unit, St. Michael's Hospital, Toronto).

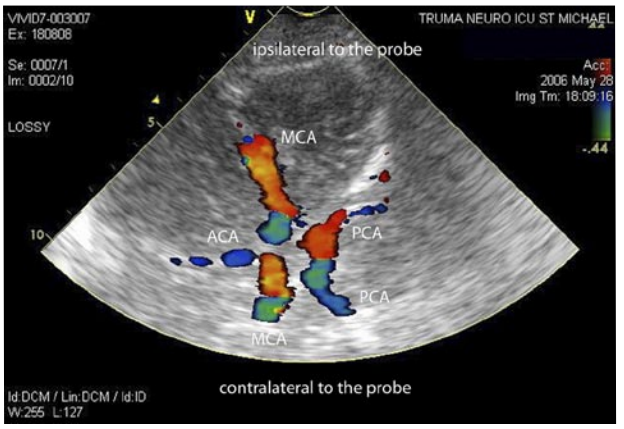

FIGURE 3 Transcranial colour-coded duplex sonography image of the basal cerebral circulation in the axial plane. Ipsilateral and contralateral anterior (ACA), middle (MCA), and posterior (PCA) cerebral arteries are clearly visualized.

ducible,[36] since it ensures that changes in flow are not due to hemodynamic changes, nor to differences in sampling area (Figure 4). A machine able to perform duplex sonography is required in order to perform TCCS. Transcranial colour-coded duplex sonography has been routinely used in our centre for vasospasm monitoring since January 2006 (Figure 5).

Doppler indices

The transcranial Doppler provides a number of ways to measure the flow patterns of cerebral arteries. The main parameters are mean flow velocity (FVm), peak systolic flow velocity (FVs), and end diastolic flow velocity (FVd). These velocities tend to decrease as age increases.[37] These values can be used to calculate the pulsatility index (PI = (FVs - FVd) / FVm) and the resistance index (RI = (FVs - FVd) / FVs) of the vessel. Evidence indicates that the PI has a strong correlation with the intracranial pressure and it is thought to be an indicator of resistance in the distal vasculature.[38] The RI provides the technician with another way of measuring downstream vascular resistance. Both of these indices tend to increase as age increases.[37]

The Lindegaard index is a ratio that helps normalize the flow velocities between patients. In mild SAH-induced vasospasm, there is concern that mild elevations of blood flow velocities may not be secondary to the local vasospasm, but to an increase in systemic flow velocities. The Lindegaard index (FV_{MCA}/FV_{ICA}) is calculated by referencing the middle cerebral artery (MCA) FV with the FV of the extracranial, ipsilateral, internal carotid artery. [34,39] In dealing with mild

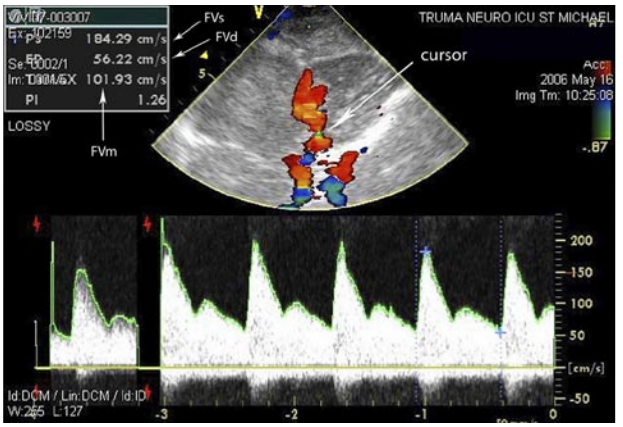

FIGURE 4 Transcranial colour-coded duplex sonography image of the basal cerebral circulation in the axial plane. During transcranial Doppler investigation, the cursor is moved along the target artery to find the highest flow velocity (top). Pulsed wave Doppler of the middle cerebral artery (MCA) at the point where the cursor is positioned (bottom). Systolic (FVs), diastolic (FVd), mean (FVm) flow velocity, and pulsatility index (PI) at top left of the screen.

to moderate MCA vasospasm, the Lindegaard ratio threshold of 3.6 was more accurate than using a mean threshold velocity of 94 $cm \cdot sec^{-1}$,[10] whereas a ratio greater than 6 is indicative of severe vasospasm. Additional experiments have been performed to modify the Lindegaard index so that it can be used when monitoring basilar artery (BA) vasospasm.[40]

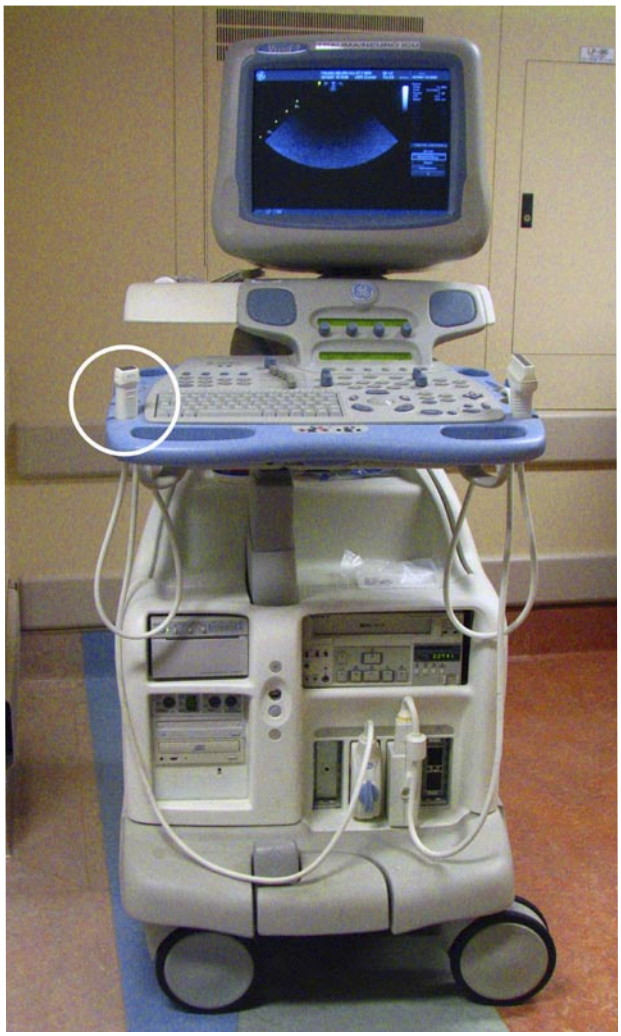

FIGURE 5 Colour-coded duplex sonography. The probe is shown in the white circle (Property of Trauma Neuro Critical Care Unit, St. Michael's Hospital, Toronto).

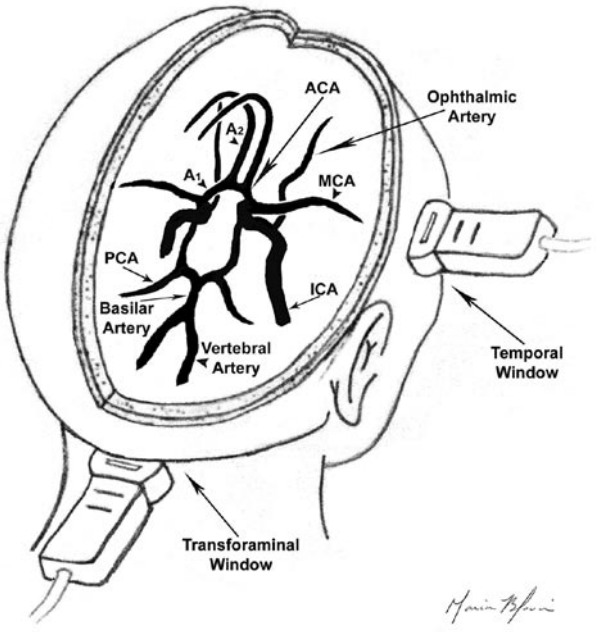

FIGURE 6 Position of the probe for transcranial Doppler investigation through the temporal or the transforaminal window and anatomical diagram of the Circle of Willis. ACA = anterior cerebral artery; A_1 = pre-communicating ACA; A_2 = post-communicating ACA; MCA = middle cerebral artery; PCA = posterior cerebral artery; ICA = internal carotid artery.

Doppler ultrasound detects vasospasm by assuming that an increased FV is a sign of arterial narrowing, thus decreased perfusion. Unfortunately, TCD does not provide estimation of cerebral blood flow and FV measurements cannot be used as a surrogate of cerebral blood flow.[41–43] McGirt *et al.*[44] showed that, in nearly 70% of SAH patients, vasospasm detected with TCD occurred, on average, 2.5 days before the appearance of delayed neurological deficits. This suggests that earlier recognition of vasospasm using TCD could result in earlier interventional treatment, with the potential for improved patient outcomes.[44]

Although it is a useful bedside tool for vasospasm monitoring, TCD may be used to monitor a wide variety of other conditions in the brain, such as internal carotid stenosis, intracranial arterial stenosis, arteriovenous malformations, intracranial expansive lesions, asphyxia, brain trauma, brain death, hydrocephalus, cerebral vasculitis, venous sinus thrombosis, sickle cell disease, and vein of Galen malformation. [33,45] Transcranial Doppler ultrasonography may have a role in "active" monitoring during procedures, such as carotid endarterectomy, emphasizing its potential for clinical impact.[33]

Transcranial Doppler ultrasonography and related neuroanatomy

A layer of diploë between two layers of compact bone forms the skull. The main obstacle for ultrasound is the diploë, because of its porous structure with many acoustic interfaces. Nevertheless, the thickness of the two layers of compact bone affects ultrasound absorption. Thinner areas of skull, called "acoustic windows", make TCD possible.

TABLE II Blood flow velocities, pulsatility index, resistance index, and diameter of basal cerebral arteries

	Flow velocity (cm·sec^{-1})					*Diameter*
	(mm)	*Peak*	*Mean*	*ED*	*PI*	*RI*
ACA	80-90	50-60	30-40	0.76-0.92	0.53-0.59	1.6-2.1
MCA	90-110	55-75	35-55	0.81-0.97	0.54-0.62	2.0-4.0
PCA (P1)	66-81	42-53	26-33	0.78-0.97	0.53-0.60	2.0-3.0
PCA (P2)	68-71	42-53	26-32	0.77-0.97	0.53-0.60	2.0-3.0
Basilar	54-74	35-50	23-34	0.77-0.95	0.51-0.60	3.2-4.4
Vertebral	52-66	33-44	22-31	0.78-0.94	0.53-0.59	3.0-4.2*

ACA = anterior cerebral artery; MCA = middle cerebral artery; PCA = posterior cerebral artery; P1 = pre-communicating PCA; P2 = post-communicating PCA; ED = end diastolic; PI = pulsatility index; RI = resistance index. *Right and left vertebral arteries usually have different size.

The temporal bone, located just above the zygomatic arch (Figure 6), is the most commonly used acoustic window. This thin portion of the skull allows an appropriate view of the flow velocities of the middle cerebral (MCA), the anterior cerebral (ACA), and the posterior cerebral (PCA) arteries. The MCA has two major branches (M1 and M2) and has a normal lumen diameter of 2–4 mm. Using TCD, the MCA can usually be found 45–65 mm away from the surface, with its distal segments 45–55 mm away. After identifying the MCA, the bifurcation of the internal carotid artery (ICA) is found by following the vessel toward the Circle of Willis. Its location is at the cranial extremity of ICA where it branches into the M1 segment of MCA and the A1 segment of ACA, and it is usually identified at a depth of 60–70 mm. The flow of MCA runs towards the surface of the temporal window (red signal), whereas the ACA, seen at the same level as the MCA, is differentiated, because it is found anteriorly and has flow coursing away from the temporal window (blue signal). Once the ICA bifurcation has been identified, the A1 (pre-communicating) and A2 (post-communicating) ACA segments can be recognized down to 70–75 mm. The pre-communicating segment (P1) of PCA can be identified behind ICA siphon at a depth of 65–70 mm from skin surface and it appears red on colour Doppler images.

The orbital window, just over the eyelid, allows the assessment of the ophthalmic artery FV, indicated by a red signal found at 40-55 mm from the surface, as well as other intra-orbital vessels.

Lastly, there is the sub-occipital or transforaminal window, located at the level of the foramen magnum (Figure 6). It is here where the two vertebral arteries (VA) enter the skull and course together at midpoints to form the BA.[33] The extracranial portion of VA and the first portion of the intracranial VA are first identified at a depth of 55–70 mm. The BA, recognized by its higher diastolic FV compared to VA, lies at 75–120 mm from the transducer surface. The sub-mental window allows an expert operator to identify the furthermost extracranial portion of ICA.

Each cerebral artery has a unique range of velocities, due to the normal variation in lumen diameter. In Table II, we report the normal ranges of blood flow values and indices of the basal cerebral arteries that Martin *et al.*[46] published in a study performed with TCCS. After correction for the angle of insonation, he determined flow velocities, pulsatility, and resistance indices in the ACA, MCA, PCA, VA, and BA in 115 volunteers.

Transcranial Doppler and vasospasm

Vasospasm is a common event after SAH, usually occurring four to 17 days after onset of bleeding. Mean MCA flow velocity (FVm) is directly correlated with narrowing grade. Indeed, Sloan *et al.*[47] showed a statistically significant correlation between FVm and the angiographic lumen diameter of MCA. Similarly, Lindegaard *et al.*[39] demonstrated an inverse relationship between MCA diameter and MCA FV.

A FVm, up to 120 cm·sec^{-1}, correlates with mild angiographic vasospasm (< 25% narrowing). A FVm, ranging between 120 and 200 cm·sec^{-1}, corresponds with a 25 to 50% narrowing (moderate vasospasm) and a FVm, higher than 200 cm·sec^{-1}, is considered severe vasospasm (narrowing > 50%).[19,48,49] Using similar criteria in a random selected cohort study of 50 patients, McGirt[44] showed that TCD defined vasospasm preceded delayed neurological deficits 64% of the time. This increase in FV, associated with severe vasospasm, can usually be detected with high sensitivity and specificity, up to two days before symptom onset.[19,47,49–51] A review by Bazzocchi *et al.*[33] reported that, for vasospasm detection, TCD sensitivity ranges from 68–94% and the specificity is between 89–100. In a meta-analysis recently published, Lysakowski[52] showed that TCD is not likely to indicate vasospasm when the angiography does not show one (high specificity), and it may be used to identify patients with vasospasm (high positive predictive value).

Ekelund *et al.*[53] demonstrated that FVm of >120 cm·sec^{-1} were slightly indicative of vasospasm, but they could not demonstrate a strict correlation between high TCD flow velocities and the occurrence of ischemic symptoms. Nevertheless, a rapid increase of 50 cm·sec^{-1} or more over a 24-hr period seemed to be a strong predictor of symptomatic vasospasm.[54] Other authors suggest that relative increases of > 25 cm·sec^{-}

^{1}·day^{-1} are an acceptable warning of the development of vasospasm.[16,55]

In a study recently published, Mascia *et al.*[50] showed that a MCA FVm threshold of 160 cm·sec^{-1} discriminated between patients with, and without, clinical vasospasm with a sensitivity and specificity equal to 1.00. The results of this study support the daily use of the TCD by trained operators, to provide early identification of SAH patients at high risk of delayed cerebral ischemia.

Krezja *et al.*[56] studied neurosurgical patients scheduled for cerebral angiography. They obtained angle corrected cerebral blood FV, pre- and post-angiography, from 214 patients. In this study, patients with vasospasm were divided into two groups (mild and moderate-severe). Krezja *et al.* suggested that, although the accuracy of TCD is high in identification of MCA spasm, standardization of FV with respect to age and sex increases the accuracy of TCD in diagnosing mild MCA vasospasm. Unfortunately, they failed to demonstrate the same increase in accuracy in the moderate-severe vasospasm group. Lastly, other studies have shown that patients with low flow velocities of deep basal veins, in conjunction with raised MCA flow velocities by TCD, appear to have worse outcomes. Therefore, the basal vein TCD is another potential method of measuring impending ischemic events.[57]

The use of TCD in vertebro-basilar vasospasm following SAH is a recent area of study that has not been fully elucidated, but appears to have some utility.[15,33,40,58–62] Studies by Soustiel *et al.*[58,60] showed that vertebro-basilar vasospasm following post-traumatic SAH appeared to independently influence neurologic outcome. Therefore, TCDs, and other imaging procedures, may be useful to follow vasospasm progression, with the intention of giving prophylactic treatment. Furthermore, evidence indicated that BA vasospasm was more common in traumatic SAH, when compared to spontaneous SAH (59.7% *vs* 40.3%).[61] When flow velocities of the BA exceeded 85 cm·sec^{-1}, it was further shown that significantly more patients experienced delayed neurological deficits.[58] Sviri *et al.*[62] demonstrated similar results, except they found that SAH basilar flow velocities > 115 cm·sec^{-1} resulted in increased risk of delayed brainstem ischemia.

An approach to the use of TCD in vasospasm

Our approach to the problem of vasospasm and the application of TCD is as follows: To begin with, all patients at risk of vasospasm receive prophylaxis (nimodipine and an attempt to establish a positive sodium balance), aimed at maintaining a euvolemic state. Patients receive regular physical examinations and beginning from day one, twice daily routine TCD evaluations in order to establish baseline velocities.

If the clinical examination is normal and remains normal, TCDs, nimodipine, and euvolemia are maintained. If the clinical examination becomes abnormal, a CTA or cerebral angiogram is performed to confirm the diagnosis. A trial of triple-H therapy (raising mean arterial pressure, volume loading) is instituted and, if unsuccessful, angioplasty is performed. If the physical examination is normal and TCD indices suggest that vasospasm is likely, we increase our vigilance with physical examinations and protocols that maintain a positive sodium. A low threshold for CTA or angiography is applied, and can be justified for confirming the previously secured aneurysm.

If the physical exam is difficult or obscured, and the TCD indices suggest the presence of vasospasm, a CTA or angiogram is performed. If vasospasm is confirmed, a trial of triple-H therapy is undertaken and, if unsuccessful, the patient proceeds to angioplasty. The clinical grade and Fisher grade suggest a risk of vasospasm and, in those who are at increased risk, TCD indices of vasospasm (even without a change in the physical exam) are used to progress from prophylaxis (nimodipine, positive sodium balance) to a trial of treatment (raised mean arterial pressure, fluid boluses), while awaiting confirmation of the diagnosis.

In any scenario where triple-H therapy is being used for demonstrated vasospasm, the degrees of TCD indices of vasospasm (as well as the physical findings) are used as an ongoing guide to the degree of triple-H employed. In these ways, use of the daily TCD has become integral to our multifaceted approach to vasospasm detection and management.

Limitations of the TCD

Although TCD appears to be a valid tool at the intensive care unit bedside, there are limitations that must be acknowledged. Transcranial Doppler ultrasonography is highly operator-dependent. Experienced TCD operators must be employed in order to ensure that proper, consistent recordings are acquired from the proper vessels and through the proper ultrasonography windows. Even where proper technique is utilized, some studies refute the existence of a strict correlation between high TCD flow velocities and occurrence of delayed ischemic deficits, indicating a need for further clinical evaluation.[53] Moreover, a small proportion of subjects (8%), especially women and older patients, do not have an adequate acoustic window.[34,63] It has even been proposed that a suboptimal window may partially account for false negative TCD results.[47]

Conclusions

Vasospasm following SAH is a very important source of morbidity and mortality. Unfortunately, too often the first sign is a neurologic deficit, which may be too late to reverse. Transcranial Doppler is a tool which adds to the constellation of important clinical information aimed at early detection, early intervention, and guiding intervention designed to prevent the permanent, neurologic sequelae related to cerebral vasospasm.

Transcranial Doppler is a relatively new, non-invasive, bedside tool that can be used to determine flow velocities in cerebral arteries. In turn, assessment of these velocities contributes valuable information regarding the diagnosis of cerebral vasospasm and, thereby, assists in clinical decision-making regarding the need for further diagnostic tests and therapeutic interventions. The current applications must be considered within the context of, and relationship to, other clinical data. When performed in isolation, the contribution of transcranial Doppler to improved patient outcome has not been established. Nevertheless, transcranial Doppler has become a regularly employed tool in neurocritical care and perioperative settings.

Acknowledgement

We sincerely thank Mrs. Maria Blouin, RRT, for her graphical support in creating the anatomical diagram shown in Figure 6.

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