

Transcranial Doppler Ultrasound

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INTRODUCTION

Transcranial Doppler ultrasonography (TCD) was introduced into clinical practice in 1982.¹ It provides a relatively cheap, portable, non-invasive and continuous estimate of cerebral blood flow (CBF) based on blood velocity.² TCD is particularly useful for demonstrating relative changes in flow, although technical limitations must be considered when interpreting results. Due to increasing expertise, an expanding body of literature and evolving technology, the clinical role of TCD is becoming more clearly defined.

PRINCIPLES

An understanding of the underlying principles provides a foundation for the appropriate application and interpretation of TCD. Range gated, pulsed wave, low frequency ultrasound is used to calculate flow velocity within selected intracranial and extracranial arteries. Typically, two MHz ultrasound is used to penetrate the bony vault via specific acoustic “windows”.³ Whilst blood velocity can be readily recorded, it should be recognised that anatomical images have relatively poor resolution. The probe emits pulsed wave ultrasound to an area of enquiry 10-15 mm in diameter, referred to as the sample volume. The sample volume is a known and adjustable distance from the probe, giving rise to the term “range-gating”. The frequency shift measured in reflected ultrasound allows calculation of flow velocity in this window using the Doppler principle.

Data undergoes fast Fourier transformation and is displayed as a spectral waveform with height proportional to velocity. Thus, the displayed image looks similar to an arterial waveform. The preferred units are cm/s rather than Hertz (referring to change in frequency). Considered more physiologic, cm/s allows measurements from

instruments using different emission frequencies to be compared.³ The depth, sample volume, power, gain and velocities are usually numerically displayed. A number of parameters (e.g. Gosling pulsatility index) have been derived to estimate factors such as downstream resistance.

Flow velocity

Under normal circumstances, the calibre of the major (or basal) cerebral arteries insonated by TCD is assumed to remain constant.^{4,5} Therefore, the measured velocity is proportional to flow. Clinically, the diameter of insonated vessels is unknown but proportional changes in velocity reflect proportional changes in flow and so real-time estimates of changes in CBF can be made.^{4,6,7} Accurate interpretation of TCD requires an understanding of when this assumption is valid, as small changes in diameter may also occur in basal arteries and become sources of error.⁸

Cerebral metabolic rate and systemic blood pressure have little impact on this assumption. Metabolic and pressure autoregulation of the cerebral circulation occurs largely at the arteriolar level. The change in calibre involves vessels 400 μm in diameter or less which are "downstream" from the vessels insonated by TCD.⁸

During steady state anaesthetic conditions, it is acceptable to interpret changes in flow velocity as changes in CBF, although controversy still exists.^{4,5} The intravenous agents do not appear to affect the basal vessels. Most but not all the evidence suggests that inhalational agents have negligible effects on the diameter of the conductance vessels and thus have little impact on the accuracy of TCD measurements.⁴ The same can be said for some other vasoactive drugs. Sodium nitroprusside and phenylephrine, for example, do not significantly affect proximal MCA diameter.

There are some pathophysiological circumstances (e.g. cerebral artery vasospasm) in which the calibre of basal arteries is known to change. Some vasoactive drugs, such as GTN, are known to cause basal artery vasodilatation in healthy volunteers.^{4,5} Furthermore, other physiological, pathological and technical factors may also affect measured TCD velocities. These are broadly classified in Table 1.

Table 1
Factors affecting TCD flow velocity

<i>Physiological</i>	<i>Pathological</i>
ICP	
Cerebral blood flow	Vasospasm
Cerebral metabolic rate	Stenosis
CO ₂ levels	
Haematocrit	<i>Pharmacological</i>
Age	GTN
Collateral flow patterns	
Body temperature	<i>Technical</i>
	Angle of Insonation

Insonation angle

Unless the ultrasound beam is directed along the axis of flow, a difference exists between the measured and true velocities. The true velocity is proportional to the cosine of the angle of insonation, so the relationship is non-linear. Using the Doppler principle, the measured velocity is always lower than or equal to the real flow velocity.⁹ Using an insonation angle of less than 30°, the error is between 0-13.5%. At 60°, the

error is 50%.³ Angle of insonation must therefore be minimised. It exceeds 30°, however, for approximately 25% of vessels insonated.⁸ This highlights the need to insonate vessels at similar angles if serial measurements are to be reliable. Insonation angle limitations, combined with restricted acoustic windows, render many intracranial vessels inaccessible to TCD.

Examination

Natural foraminae and relatively thin areas of the cranium are used to access the intracranial vasculature. Specifically, the transtemporal (anterior, middle, posterior cerebral arteries), transorbital (carotid syphon, ophthalmic artery) and suboccipital (basilar, vertebral arteries) routes are used. The temporal window permits insonation of the proximal segment (M1) of the middle cerebral artery (MCA) in 90% of people.⁴ Younger subjects generally have larger windows, making studies technically easier to obtain.¹⁰ Advancing age, female gender and African descent are factors associated with smaller acoustic windows, leading to failure rates as high as 20-30% in these populations.^{2,4,8,10} About 75-80% of the carotid artery blood flow passes through the ipsilateral MCA, making the MCA representative of hemispheric blood flow and a key vessel for TCD analysis.⁴

Handheld probes can be used to perform brief studies to scan the cerebral circulation. For prolonged monitoring, and to ensure a constant angle of insonation over time, various devices allow the fixation of probes over the temporal window for monitoring of up to four vessels simultaneously.

Vessel Identification

Characteristics such as the acoustic window, vessel depth, direction of flow, relative flow velocities, spatial relationship to the MCA/ACA bifurcation and response to ipsilateral carotid artery compression are all used to discriminate between vessels.¹⁰ Distinct visual waveform contours and audio feedback may assist in localisation of vessels and optimisation of signal.¹⁰ A knowledge of the relevant anatomy is important.

It is clear, therefore, that TCD is not a “set and forget” monitor. It requires skill and expertise to allow mapping of elements of the cerebral circulation and the signals must be considered in the clinical context. Nevertheless, it is a valuable tool. The applications of TCD for clinical practice are discussed below.

APPLICATIONS OF TCD

In 1990 the American Academy of Neurology (AAN) reported that TCD was of established value in the assessment of intracranial stenoses, collateral circulation, cerebral vasoconstriction (especially after subarachnoid haemorrhage), arteriovenous malformations and brain death.¹¹ Numerous other applications have been investigated. In 2000, with the endorsement of the American Society of Neuroimaging and the Neurosonology Research Group of the World Federation of Neurology, a panel of 11 international experts issued an evaluation of the clinical utility of TCD.⁸ It followed the AAN “Format for an Assessment” and incorporated personal experience, solicited opinions, extensive Medline searches and literature reviews.

Ischaemic cerebrovascular disease

Intracranial atherosclerosis accounts for up to 10% of strokes and transient ischaemic attacks. TCD criteria for the diagnosis of intracranial stenosis includes

circumscribed flow velocity increase, distal signal damping and side to side differences in velocity.⁸ Signal absence from an artery in the presence of signals from other vessels insonated through the same window and signs of collateral flow suggest vessel occlusion. The international panel recommended TCD as being of established value for the detection of intracranial atherosclerotic lesions as well as the evaluation of patients with internal carotid artery disease based on class II evidence (provided by one or more well-designed clinical studies).⁸

TCD has been used to identify acute cerebral arterial occlusion, monitor arterial recanalisation and evaluate the risk of haemorrhagic transformation of large volume ischaemic lesions.⁴ Some centres use serial TCD to guide thrombolytic therapy.^{8,12} TCD is of established value for the evaluation of patients with acute cerebral infarction, based on class II evidence.⁸

Embolism

TCD will detect both gaseous and solid emboli.² Formed element emboli produce high intensity transient signals (HITS) which move within the spectral envelope and with the direction of flow. Artifacts are bidirectional and have maximum intensities at low frequencies.⁸ Asymptomatic emboli are common in the presence of known carotid artery stenosis and may be an independent predictor of future stroke risk.² They may localise an embolic source and provide a surrogate endpoint in the evaluation of novel therapies.^{2,8} There is strong evidence that TCD can detect cerebral microembolisation. Babikian et al concluded that the clinical usefulness of this detection required more study before a definite recommendation could be given.⁸

Vasospasm and Subarachnoid Haemorrhage

A variety of central nervous system disorders may induce cerebral vasospasm, or contraction of the intracranial arteries. Cerebral ischaemia may occur, leading to transient or permanent neurological dysfunction. Vasospasm is the leading cause of morbidity and mortality in patients who initially survive an aneurysmal subarachnoid haemorrhage (SAH), even after the aneurysm has been secured surgically or radiologically.^{4,13} It occurs in 70% of all patients presenting with aneurysmal SAH and leads to symptomatic brain ischaemia or infarcts in up to 36% of all patients.^{8,13} Mortality in the first 2 weeks after SAH increases 150-300% in the presence of vasospasm.¹³

Various time courses have been described.¹⁴ Generally, vasospasm requires 4 days to develop and resolves by day 17.¹² The pathogenesis is not precisely known, although it appears to be related to the presence of subarachnoid blood. Prolonged smooth muscle contraction is mediated by extravasated oxyhaemoglobin.⁴ The process may be focal or diffuse.¹² Secondary morphological changes such as intimal hyperplasia or sub-endothelial fibrosis can follow. Although once regarded as the major cause of lumen narrowing, these changes are now considered delayed and nonspecific responses to cerebral vasospasm, appearing after its resolution.¹³

The haemodynamic effects of vasospasm are similar to that of a stenosis — an increase in blood flow velocity and a loss of pressure occur through the narrow segment. Initially, cerebral blood flow will be maintained by dilatation of the distal vascular bed but, when the compensatory effects of collateral circulation and distal autoregulation are exhausted, critical reductions in CBF can occur.¹⁵

Causes of cerebral vasospasm include SAH, trauma, meningitis and pre-eclampsia,

and all can be associated with ischaemic cerebral damage. In the presence of basal artery vasospasm, flow velocity can no longer be used to infer cerebral blood flow. Although the assumption of unchanging vessel calibre is no longer valid, TCD still provides important clinical information regarding the presence and time-course of vasospasm. TCD diagnosis in patients at risk for vasospasm depends on:

1. Absolute velocities (MFV-MCA >120 cm/s)
2. Relative rise (>50 cm/s/d)
3. Hemispheric index or Lindegaard ratio (MCA/ICA velocity ratio >3)

Normal mean flow velocity (MFV) in the MCA is 30-80 cm/s.¹⁵ Mean velocities above 120cm/s are associated with mild to moderate angiographic vasospasm.^{12, 13} MFV above 200 cm/s suggest severe vasospasm (more than 50% diameter narrowing), although some patients may remain asymptomatic.^{8, 12, 13, 14, 15} Intermediate velocities may have poorer predictive value of angiographic and symptomatic vasospasm than lower (<120 cm/s negative) or higher (>200 cm/s positive) velocities.¹³ Early, rapid development of severe spasm is associated with an increased risk of cerebral infarction.^{8, 12, 13, 14, 16} An early rise in MFV-MCA (≥ 110 cm/s on or before day 5 post SAH) is an independent predictor of symptomatic vasospasm. Predictive value is higher ($68 \pm 8\%$) when combined into a "symptomatic vasospasm risk index".¹⁶

Increased MFV due to vasospasm/stenosis can be distinguished from that due to hyperaemia by the MCA/extracranial ICA velocity ratio, which is normally 1.7 ± 0.4 . Lindegaard et al demonstrated that a ratio >3 suggests vasospasm (ratio >6 indicates severe vasospasm).¹⁴

TCD is most reliable in detecting MCA vasospasm (sensitivity 75-90%, specificity >90%), as well as that of the vertebral and basilar arteries. Collateral flow patterns render it unreliable in detecting vasospasm of the anterior cerebral arteries (ACA).^{8, 12} The TCD effects of haemodynamic therapy and nimodipine are not well studied although higher velocities have been recorded even in the absence of vasospasm.^{13, 14}

While conventional and digital subtraction cerebral angiography are the standard techniques used to diagnose vasospasm, they are invasive and associated with significant morbidity.⁸ It is clear that TCD is valuable for the non-invasive and early diagnosis of vasospasm, before the onset of ischaemic symptoms, which can allow the early institution of appropriate treatment regimens and thus potentially the prevention of irreversible damage.⁴ The Babikian group gave TCD a positive recommendation based on class II evidence.⁸ Daily, or alternate day TCD assessment has been advocated.^{4, 12} Monitoring is particularly useful between days 4-10 or until spasm diminishes to low moderate levels or less.⁸ CBF imaging techniques such as xenon computed tomography (Xe CT) and single-photon emission computed tomography (SPECT) in conjunction with TCD assessment may be helpful in directing therapy.^{8, 17}

The treatment of vasospasm includes induced hypervolaemia, hypertension, haemodilution (TripleH therapy) and the administration of cerebral selective calcium channel antagonists. The rationale is that, in areas supplied by affected vessels, cerebral blood flow regulation is impaired and becomes pressure-dependant.¹³ These interventions have potentially life threatening complications, such as cardiac failure, electrolyte abnormalities, catheter related problems, rupture of an unsecured aneurysm or exacerbation of cerebral oedema.¹³ Despite the lack of robust outcome data, triple H therapy received a qualified recommendation by the Stroke Council of the American Heart Association in 1994.¹⁸ The use of nimodipine was strongly recommended to reduce poor outcome related to vasospasm.¹⁸ Intracranial angioplasty

and intra-arterial papaverine infusions are also used in selected patients, particularly those refractory to medical treatment.

Cerebral circulatory arrest

Brain death is a clinical diagnosis which can be supported by TCD evidence of absent cerebral blood flow at all insonation sites.⁸ Potential patterns are low diastolic flow velocities, systolic peaks, oscillating blood flow (retrograde diastolic flow), short systolic spikes, and absent TCD signals.¹² These patterns are similar to those observed with severely elevated intracranial pressure and several caveats apply. Monitoring should continue for at least 30 minutes at normal body temperature.⁸ Repeated measures improve reliability. Flow velocity differences of more than a few cm/s may indicate a technically inadequate study. Only loss of a previously identifiable waveform can be interpreted as the absence of cerebral flow.¹²

TCD may facilitate shortening the observation period before organ harvest, and provide laboratory confirmation of the clinical diagnosis. There is class II evidence supporting the established value of TCD for evaluating cerebral circulatory arrest associated with brain death.⁸

Arteriovenous Malformations

Arteriovenous malformations (AVM) are developmental anomalies with direct communication between arteries and veins. Without vasomotor arterioles and capillaries, these vessels are characterised by high blood velocity, low pulsatility, low perfusion pressure and decreased CO₂ reactivity.⁴ AVMs may cause intracerebral haemorrhage, seizures, or both.⁸ Treatment includes endovascular embolisation, radiotherapy and surgical removal. Differentiation between healthy and AVM “feeder” vessels is important.

The evidence for TCD assessment of AVMs consists of small, non-blinded series, which lack randomised controls (class III).⁸ The Babikian group concluded that TCD was unacceptable as a screening test, but is effective in identifying supply arteries to medium or large AVMs. It is effective in assessing staged embolisation or resection of AVMs.⁸

Perioperative monitoring

Stroke is both the major indication for carotid endarterectomy and its major complication.⁴ The majority of perioperative strokes are embolic, but optimisation of cerebral perfusion during cross clamping is considered desirable.^{4,8} Shunt insertion increases stroke risk and is avoided where possible.⁴

TCD can be used to monitor ipsilateral MCA and thus provide an endpoint for treatment regimes such as optimal perfusion pressure or the need to shunt. Stroke rate is increased with initial fall in MFV to $\leq 15\%$ pre-clamp value and with persistent decrease to $<40\%$ baseline after 5 minutes. A post-clamp reduction in MFV-MCA to less than 40% baseline is a commonly accepted indication for shunt.⁴ Postoperatively, HITS monitoring to detect and count emboli can be performed. Furthermore, TCD can detect kinked or thrombosed shunts.^{4,8}

With a strong consensus of class III evidence, the panel gave TCD a positive recommendation for use during and after carotid endarterectomy. It was considered investigational during cardiac surgery, but overall received a “promising” rating for perioperative monitoring.⁸

Sickle cell disease

Arterial stenotic lesions and cerebral infarction are common complications of sickle cell disease.¹⁹ Time averaged maximum mean flow velocity of 200 cm/s or greater in MCA or intracranial internal carotid artery is strongly associated with an increased risk of stroke in neurologically asymptomatic children. Prophylactic blood transfusion in these patients reduced relative risk of ischaemic stroke by 90%.²⁰ The National Heart, Lung and Blood Institute has issued a clinical alert recommending that sickle cell patients between the ages of 2 and 16 receive TCD screening.¹⁹ This is the strongest evidence for the effective clinical application of TCD.

Autoregulation and vasomotor reactivity

Cerebrovascular responses can be impaired with some pathological conditions (e.g. closed head injury) and definition of these responses may be critical in determining therapeutic strategies such as deliberate hypertension. The integrity of cerebral autoregulation can be evaluated using TCD. Good temporal resolution reflects changes as they occur. The limits of pressure autoregulation are delineated using dynamic or static techniques. Dynamic recovery after a rapid transient decrease in mean blood pressure is measured after deflation of large thigh cuffs.⁴ Static response to vasopressor infusion has also been used.⁴

Vasomotor reactivity (VMR) is tested using changes in flow velocity in response to acetazolamide injection, hyperventilation, or CO₂ inhalation.^{2,8} Flow velocities may drop 35% with hyperventilation and increase 50% with hypercapnia in healthy patients.⁸ Maximally dilated vessels are refractory to dilator stimuli and exhibit no increase in flow velocity. This indicates that vasomotor reserve is exhausted and a fall in perfusion pressure, for whatever reason, may lead to an ischaemic brain injury.²¹ Diminished vasomotor reactivity has been associated with an increased risk of stroke in patients with severe extracranial internal carotid disease.^{2,8} Although the testing of VMR has only limited clinical applications, TCD is considered useful for the evaluation of vasomotor reactivity on the basis of class III evidence.⁸

Other Applications

Among the other major applications reviewed, TCD was considered promising for the evaluation of patients with meningeal infection. It received negative ratings for periprocedural monitoring (e.g. angiography), migraine and the assessment of central venous thrombosis, where it was regarded as investigational.⁸

TCD TRAINING

TCD is operator dependent. Accurate acquisition and interpretation of data requires knowledge, skill, and experience. An understanding of the clinical context is important. The American Academy of Neurology and the American Society of Neuroimaging have recommended certification of physicians performing or interpreting TCD studies, and endorsed guidelines for training.⁸ It has been suggested that about 200 examinations are required to gain familiarity with the technique.²²

DEVELOPMENTS

Echo-contrast enhancing agents have facilitated the combination of Doppler blood flow imaging with B-mode tissue imaging (transcranial colour-coded duplex or TCCD).^{2,22} These microbubble preparations survive cardiopulmonary and capillary

transit and increase the signal to noise ratio by a factor of 1000.²³ The failure rate due inadequate acoustic window is reduced.²³ Spatial resolution is enhanced allowing visual identification of vessels, sampling of defined volumes within the vessel and calculation of angle-corrected flow velocities.^{2, 22} The principle application of TCCD is in the evaluation of cerebrovascular status in stroke patients.²³ The use of contrast agents during TCD was deemed investigational by Babikian et al.⁸

SUMMARY

Transcranial doppler provides a non-invasive estimate of cerebral blood flow based on flow velocity. Its advantages and disadvantages are summarised in Table 2. In the hands of skilled operators, real time investigation of cerebral haemodynamics is possible at the bedside. Despite a number of technical limitations, TCD has an established role in the evaluation of ischaemic cerebrovascular disease, subarachnoid haemorrhage, arteriovenous malformations and cerebral circulatory arrest. It is effective in the evaluation of sickle cell disease and shows promise as a perioperative monitor, particularly for carotid endarterectomy.

Table 2
Advantages and disadvantages of TCD

Advantages	Limitations
effective	operator dependant
noninvasive	skilled personnel required
uses small, portable equipment	patient must lie still
relatively inexpensive	technical limitations including acoustic window, angle of insonation
repeatable	poor spatial resolution
safe	
good temporal resolution	

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