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REVIEW

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Applications of transcranial Doppler in the ICU: a review

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Abstract *Objective:* Transcranial Doppler (TCD) ultrasonography is a technique that uses a hand-held Doppler transducer (placed on the surface of the cranial skin) to measure the velocity and pulsatility of blood flow within the intracranial and the extracranial arteries. This review critically evaluates the evidence for the use of TCD in the critical care population. *Discussion:* TCD has been frequently employed for the clinical evaluation of cerebral vasospasm following subarachnoid haemorrhage (SAH). To a lesser degree, TCD has also been used to evaluate cerebral autoregulatory capacity, monitor cerebral circulation during cardiopulmonary bypass and carotid endarterectomies and to diagnose brain death. Technological advances such as M mode, colour Doppler and three-dimensional power Doppler ultrasonography have extended the scope of TCD to include other non-critical care applications including assessment of cerebral emboli, functional TCD and the management of sickle cell disease. *Conclusions:* Despite publications suggesting concordance between TCD velocity measurements and cerebral blood flow there are few randomized controlled studies demonstrating an improved outcome with the use of TCD monitoring in neurocritical care. Newer developments in this technology include venous Doppler, functional Doppler and use of ultrasound contrast agents.

Keywords Transcranial Doppler · Subarachnoid haemorrhage · Intracranial pressure · Brain death · Neurocritical care

History

In the middle 1800s Christian Andreas Doppler observed that when a sound wave with a certain frequency strikes a moving object, it is reflected with a different frequency. This phenomenon came to be known as the Doppler effect. The principle was utilized by Spencer and Reid [1] who popularized the concept of imaging blood vessels using ultrasound. In the late twentieth century Aaslid and colleagues (1982) introduced transcranial Doppler (TCD) ultrasonography into clinical practice for the evaluation of cerebral haemodynamics, ushering in a new era of cerebral circulation monitoring [2]. Their successful adaptation of ultrasound technology was due to the following factors: (a) the use of a relatively low ultrasonic frequency (2 MHz), with better bone penetration, and (b) insonation of the intracranial vessels via the temporal area, which is the thinnest part of the skull.

Basic concepts

Ultrasound technology is based on the Doppler effect [3]. The TCD probe emits a wave with known frequency f_O and propagating speed c towards a moving target and receives the echo. The echo is the reflected wave with an altered frequency *fe*. The difference in frequency between the incident and the reflected waves is known as the

Doppler shift, *fd*, and can be determined as: $fd = fe - fo$. A shift to a higher frequency is termed positive Doppler shift, and to a lower frequency is a negative shift. According to the Doppler equation for a reflector, the velocity v of the moving target can be calculated as:

$$v = \frac{c \times fd}{2 \times fo} \tag{1}$$

where c is the speed of the incident wave. This assumes that the target moves directly towards the device. If the target moves in a direction that has an angle θ (Doppler angle) towards the device, the equation becomes:

$$v = \frac{c \times fd}{2 \times fo \times \cos\theta} \tag{2}$$

If the angle ranges from 0° to 30°, its cosine varies between 1 and 0.86. Thus the maximum error due to θ will be less than 15%.

The TCD system uses this principle to measure cerebral blood flow (CBF) velocity and displays the information as a velocity-time waveform. The peak systolic (PSV) and end-diastolic (EDV) blood flow velocities (FV) are measured directly from the waveform display. The mean velocity (MV), resistance index (RI) and pulsatility index (PI) [4, 5, 6], may be calculated as follows:

$$\mathrm{MV} = \frac{\mathrm{PSV} + (\mathrm{EDV} \times 2)}{3} \tag{3}$$

$$\mathrm{PI} = \left(\frac{\mathrm{PSV} - \mathrm{EDV}}{\mathrm{MV}}\right) \tag{4}$$

$$\mathrm{RI} = \left(\frac{\mathrm{PSV} - \mathrm{EDV}}{\mathrm{PV}}\right) \tag{5}$$

TCD systems use pulsed-wave Doppler which employs a single transducer for emitting and receiving pressure waves [3]. In contrast to continuous-wave Doppler, pulses are emitted in discrete packages. The time interval during which the transducer accepts returning signals is manipulated to allow sampling from a specific range of depths. The pulse repetition frequency (PRF) describes how many pulses per second are generated [7]. The pulsed-wave beam has its energy concentrated in the pulse-duration and no energy distributed in pulse interval. Therefore the pulsed-wave beam has much greater strength per wave-unit, resulting in better penetration.

The Nyquist-Shannon sampling theorem which governs the frequency of sampling a signal also applies to the Doppler system [8]. According to this theorem, in order to perfectly reconstruct the original signal from the sampled version the sampling frequency must be at least twice the frequency of the signal itself. Furthermore, accurate depiction of a Doppler shift requires at least two sampling pulses per cycle of the shifted waveform. There is therefore an upper limit to the Doppler shifts that can be detected by pulsed Doppler instruments, the Nyquist limit. As pulse-wave equipment collects samples of waves at the rate of PRF, a pulsed Doppler device cannot accurately determine Doppler shifts exceeding PRF/2 [9].

Technique

TCD uses a hand-held microprocessor-controlled transducer. It transmits a low-frequency (2 MHz) pulse-waved ultrasonic signal from skin surface across the cranial vault to the intracerebral arteries and receives the echoes along the same path. In an adult human, cranial bones fully encase the cranial cavity, leaving only small foramina for vessels and nerves. Bone tissue heavily attenuates ultrasound with at best, only 6% of the intensity of the ultrasound reaching the brain substance.

Acoustic windows are thin areas of bone or naturally occurring foramina or fissures that allow the best transmission of TCD signal [9]. There are three naturally occurring acoustic windows: transtemporal, transorbital and transforaminal windows (Fig. 1). The transtemporal window is used to study the middle, anterior and posterior cerebral arteries. The transorbital window is used to examine the ophthalmic artery and the three segments of the cavernous portion (siphon) of the internal carotid artery.

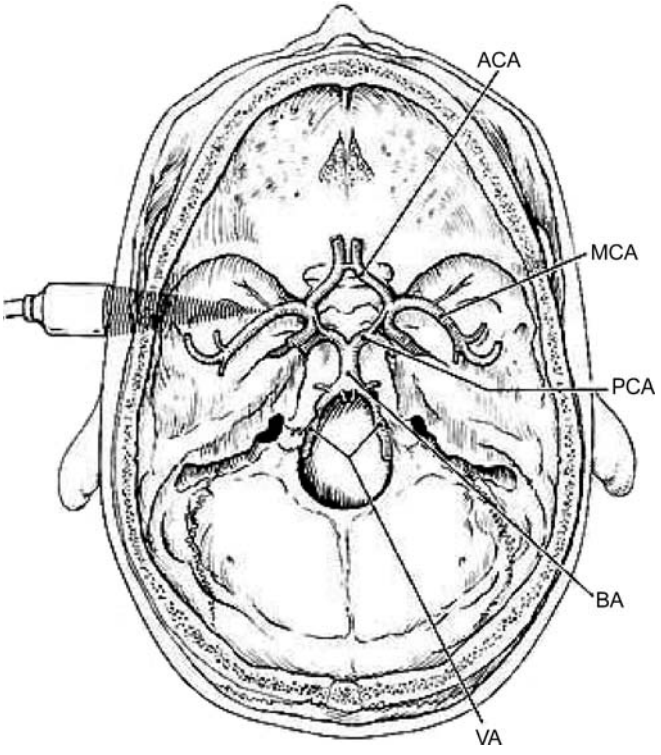

Fig. 1 The temporal window allows insonation of the anterior, middle and posterior cerebral arteries. (Reproduced with permission from [9])

The transforaminal window allows assessment of the intracranial portions of the basilar and vertebral arteries. It should be noted that up to 8% of persons do not have an adequate acoustic window [10].

In general, six factors are used to identify the insonated artery (Table 1): (a) the window through which the vessel is insonated, (b) the depth of sample volume, (c) the orientation of the transducer during insonation, (d) the direction of blood flow with respect to the transducer, (a) the relationship of the vessel to the junction of middle (MCA) and anterior cerebral arteries (ACA) and the terminal portion of the internal carotid artery, and (f) the response to dynamic maneuvers (for example, compression of the common carotid results in a temporary decrease in MCA velocity on the ipsilateral side) [9].

Systolic, diastolic and time-averaged mean values can be estimated from waveform analysis of reflected Doppler shift echoes from red blood cells. These echoes are received and converted into electric voltages that pass into the electronic component of the instrument. The signal is processed by demodulation and fast Fourier transformation and Doppler shifts are obtained and displayed in spectral form. The frequency shift is on the vertical axis and time on the horizontal. FV varies with CBF, angle of insonation, vessel diameter and collateral flow.

Normal values are influenced by a number of physiological and demographic factors. Physiological determinants of velocity are similar to those influencing CBF and include mean arterial blood pressure (MAP), partial pressure of arterial carbon dioxide ($PaCO_2$) and haematocrit. Demographic factors include age, sex, pregnancy and arousal state. At birth MCA FV is approx. 24 cm/s, increasing to 100 cm/s at the age of 4–6 years. Thereafter it decreases steadily to about 40 cm/s in the seventh decade of life. Women generally have a higher FV than men, although the difference is usually small (10–15%). During normal pregnancy FV is maintained for the first two trimesters but decreases during the third. FV drops by approximately 15% during sleep [11].

The range of normal values for adults was determined by Aaslid et al. [2]. The mean velocities obtained in the middle cerebral artery, anterior cerebral artery, and posterior cerebral circulation (PCA) were: 62 ± 12, 51 ± 12 and 44 ± 11 cm/c, respectively (Table 1). These values were in the same ranges as those found by direct Doppler techniques during surgery [12, 13]. The procedure introduced by Aaslid et al. has now been adopted by other researchers as a standard method to detect the FV of basal cerebral arteries [2, 14].

Several authors have suggested that velocities vary for each individual. Venkatesh et al. [15] measured MCA velocities continuously in healthy volunteers and patients with SAH. They demonstrated a significant moment to moment variability between flow estimates performed in the same individual, in both volunteers (–31% to +58%) and patients (–38% to +78%). This is an important finding as most published studies report intermittent FV. Intermittent TCD may potentially miss significant peaks or troughs in measurements, creating the potential for false negatives and false positives in the diagnosis of vasospasm. Another important consideration is the dynamic nature of the relationships between blood flow, velocity and pressure drop and changes in luminal diameter of vessels as described by Spencer and Reid [1]. They observed that at a high degree of stenosis there is a rapid decline in the PSV (Fig. 2). Thus PSV increases with reducing vessel diameter up to a critical value and then begins to decrease despite worsening vasospasm [16]. This needs to be borne in mind when interpreting alterations in velocities to avoid the potential for misinterpretation [17].

Calculated Indices

Lindegaard ratio

Although controversial, a mean FV above 120 cm/s is generally considered abnormal [6]. Differentiating vasospasm

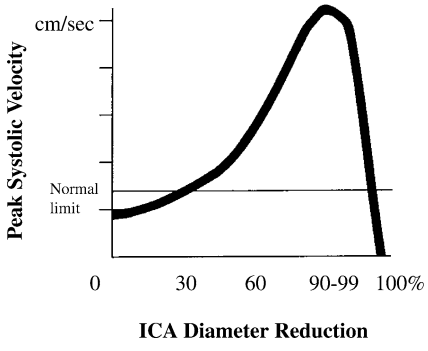

Fig. 2 Flow velocity is proportional to the degree of vessel stenosis. Spencer and Reid [17] described the relationship between velocity and vessel diameter. (Reproduced with permission from [17])

Table 1 Criteria for artery identification (*OA* ophthalmic artery, *MCA* middle cerebral artery, *ACA* anterior cerebral artery, *PCA* posterior cerebral artery, *VA* vertebral artery, *BA* basilar artery)

Artery	Window	Depth (mm)	Transducer orientation	Flow direction	Velocity (cm/s)
OA	Orbital	40–50	Slightly medial	Toward	16–26
MCA	Temporal	35–60	En face	Toward	46–86
ACA	Temporal	60–75	Anteriorly	Away	41–76
PCA	Temporal	60–75	Posteriorly	Toward	33–64
VA	Foraminal	45–75	Superiorly and obliquely	Away	27–55
BA	Foraminal	70–120	Superiorly	Away	30–57

from hyperaemia using TCD can be problematic as both conditions may result in elevated FV. In 1988 Lindegaard et al. [18] put forward an index to distinguish between the two by comparing the FV of the MCA with that of the extracranial portion of the ipsilateral internal carotid artery. They compared the estimates to cerebral angiographic assessments. The ratio of FV in the MCA to that in the external carotid artery increased with the severity of vasospasm. This ratio (Lindegaard ratio, LR) ranged from 1.1 to 2.3, median 1.7 at days 1–2, but rose to over 10 in patients with the most severe MCA lumen narrowing. In the setting of elevated FV a ratio lower than 3 is considered hyperaemia, a ratio of 3–6 mild vasospasm and a ratio higher than 6 consistent with severe vasospasm.

Pulsatility index

The most widely used measures of intracranial resistance are Pourcelot's resistance index (RI) and the pulsatility index (PI) developed by Gosling and King [4] (see also [19]). The "pulsatility" of the FV waveform reflects the resistance of the more distal cerebral vasculature. Both RI and PI are influenced by physiological factors including arterial pressure, vascular resistance and changes in $PaCO_2$. The PI has been evaluated as an alternative to direct intracranial pressure (ICP) measurement. Bellner et al. [20] compared the PI index with ICP measurements from intraventricular monitors in 81 patients with various intracranial disorders. A strong correlation was found between the ICP and the PI ($r = 0.938$, $p < 0.001$) within the ICP ranges of 5–40 mmHg. Omitting repeated measurements and considering only the initial TCD ICP recording in each subject ($n = 81$) for the interval 5–40 mmHg, the R^2 value was 0.733 ($p < 0.0001$) with an SD of 2.5. The regression line is: ICP (PI) = $11.1 \times \text{PI} - 1.43$. The correlation between the cerebral perfusion pressure (CPP) and PI was also significant but less strong ($r = -0.493$, $p < 0.001$). Similarly, the RI has been used to demonstrate the presence of raised ICP. Several authors have reported good correlation between RI and raised ICP in cases involving various intracranial pathological processes including hydrocephalus [21, 22]. Table 2 summarizes the differential diagnoses of a perturbation in the measured and calculated indices.

Table 2 Differential diagnosis of changes in flow velocity and resistivity indices during transcranial Doppler examination (from [5, 6, 18, 20, 115, 116])

Transcranial Doppler flow velocity
Increase
Vasospasm
Hyperaemia
Loss of autoregulation
↑ $PaCO_2$
Intracranial arterial stenosis
Increasing age
Hyperdynamic circulation
Volatile anaesthetic agents
Sickle cell anaemia
Arteriovenous malformation
Bacterial meningitis
Pre-eclampsia
Decrease
Hypotension
↓ CBF
Brain death
Raised ICP
↓ $PaCO_2$
↑ angle of insonation
Pregnancy
Anaesthetic Induction agents (except ketamine)
Hypothermia
Fulminant hepatic failure
Pulsatility index, resistance index
Increase
Raised ICP
Hydrocephalus
Traumatic brain injury
Intracerebral haemorrhage
Fulminant hepatic failure
Stroke
Brain death
Intracranial artery occlusion
Bacterial meningitis
Decrease
Vasospasm
Arteriovenous malformation
Rewarming following hypothermia
Hyperaemia
Lindegaard ratio
Increase
Vasospasm
Decrease
Hyperaemia

Assessment of cerebral perfusion pressure and cerebral blood flow using TCD

Relationship between TCD measurements and CPP

CPP is the difference between arterial pressure (AP) and the effective downstream pressure (EDP) of the cerebral circulation. Because of a Starling resistor phenomenon located at the level of cerebral veins ICP is thought to represent the EDP of the cerebral circulation [23]. The Brain Trauma Foundation's guidelines recommend a CPP of at least 60 mmHg [24]. Direct measurement of ICP is not always possible when the risk of a reduction in CPP is maximal, for example, during the early management of brain-injured patients. In this instance TCD evaluation of MCA velocity has been proposed as an alternative for neurological monitoring.

Several methods of estimating CPP using measured TCD velocities have been described: Aaslid et al. [25] determined CPP using the following TCD parameters:

where $F1$ and $A1$ represent amplitude of the fundamental frequency components of FV and arterial pressure, respectively. The fundamental frequency is determined by fast Fourier analysis of the waveform, and is equivalent to the heart rate.

Czosnyka et al. [26] used measured and calculated TCD variables from 96 patients with head injury to derive a different formula to estimate CPP:
using time averaged mean, systolic and diastolic values of FV from the MCA. A subsequent validation study of the above method reported the absolute difference between measured CPP and calculated CPP (daily averages) to be less than 10 mmHg in 89% of measurements and less than 13 mmHg in 92% of measurements [27].

Edouard et al. [28] investigated a simplified model of CPP originally described in pregnant patients. They compared conventional measurements of CPP (difference between MAP and ICP) with an estimated CPP (CPPe). CPPe was derived using a formula combining the phasic values of FV and arterial pressure:

$$\mathrm{CPPe} = \left(\frac{v_{\mathrm{mean}}}{v_{\mathrm{mean}} - v_{\mathrm{diast}}}\right) \times (\mathrm{AP}_{\mathrm{mean}} - \mathrm{AP}_{\mathrm{diast}}) \quad (6)$$

where v_{mean} and v_{diast} are the mean and diastolic MCA velocities, and $\mathrm{AP}_{\mathrm{mean}}$ and $\mathrm{AP}_{\mathrm{diast}}$ are the mean and diastolic arterial pressures, respectively. Twenty adults with bilateral and diffuse brain injuries were included in the study. CPPe and CPP were correlated (slope 0.76. intercept +10.9, 95% CI 3.5 to +25.4). The intercept of the regression line equaled the zero flow pressure (ZFP), in the MCA and represents the EDP of the cerebral circulation. Noninvasive measurement of CPP is a promising technique. Current evidence suggests that EDP as predicted by the critical closing pressure is as useful as ICP in describing cerebral haemodynamics, and in some instances better. Weyland et al. [29] observed that during hypocapnia cerebrovascular tone rather than ICP determines the EDP and therefore CPP. Thus MAP EDP would give a better indication of CPP in this situation. More work is needed as none of the recently described methods has been fully validated; in particular, it is not clear from the existing literature which formula is most appropriate under given pathophysiological conditions.

Relationship between TCD and cerebral blood flow

TCD velocities have been used to provide information about CBF. A number of studies have assessed the validity of comparing FV with techniques for measuring CBF, including IV xenon, the Kety-Schmidt method, magnetic resonance imaging, single photon emission computed tomography and laser Doppler flowmetry [30, 31]. Results have been inconsistent. Brauer et al. [32] compared TCD with xenon-enhanced computed tomography in 32 patients with varying intracerebral pathologies. Acetozolamide or CO_2 was used to induce a change in CBF. They observed that changes in FV were correlated well with CBF measures for the group as a whole ($r = 0.82$) but not subgroups classified according to diagnosis. Not all authors agree. Minhas et al. [33] studied cerebral perfusion patterns (positron emission tomography) and associated TCD indices in 25 patients who developed clinical signs of delayed ischaemic deficits (DID) following SAH. They identified a markedly heterogeneous pattern of CBF distribution, with hyperaemia, normal CBF values and reduced flow among patients with DID. TCD indices were not indicative of the cerebral perfusion findings. In summary, whilst the TCD represents a non-invasive method of obtaining information about CBF, the linear relationship between CBF and FV is only present if neither the diameter of the insonated vessel nor the angle of insonation change during the examination.

Clinical applications of TCD in the ICU

Subarachnoid haemorrhage

Vasospasm is a major cause of morbidity and mortality following aneurysmal SAH (Fig. 3). Clinically important vasospasm (or delayed ischaemic deficit) occurs in 20–30% of patients within 3–14 days after bleed. Angiographic vasospasm however, can be demonstrated in up to 60% of patients. Given that vasospasm is associated with significant morbidity and mortality, it is imperative not only to diagnose but also predict those patients who are likely to become symptomatic. Aaslid et al. [34] investigated the use of TCD technology for the diagnosis and management of vasospasm. An inverse relationship between vessel diameter and TCD velocities was observed. Their group went on to define mean TCD velocities higher than 120 cm/s as mild and those higher than 200 cm/s as indicative of severe vasospasm [2, 34, 35]. Several authors have confirmed the Aaslid et al. findings, but it was not until 1987 that a controlled trial was performed by Compton et al. [36, 37]. They compared the Doppler FV in three groups of patients, a SAH group, a control group and a group of patients with other cerebral pathologies. They observed that in the SAH group FV tended to be higher. In 80% of patients with MCA FV higher than 100 cm/s they demonstrated vasospasm on angiography. However, a strong correlation with the clinical grade of SAH or onset of neurological deficit was not demonstrable [37].

Comparison of TCD with angiography for detection of vasospasm

Attempts to establish a correlation between TCD velocity and angiographic vasospasm have met with mixed results. A variety of end-points have been investigated to improve sensitivity and specificity. Lindegaard et al. [18] measured

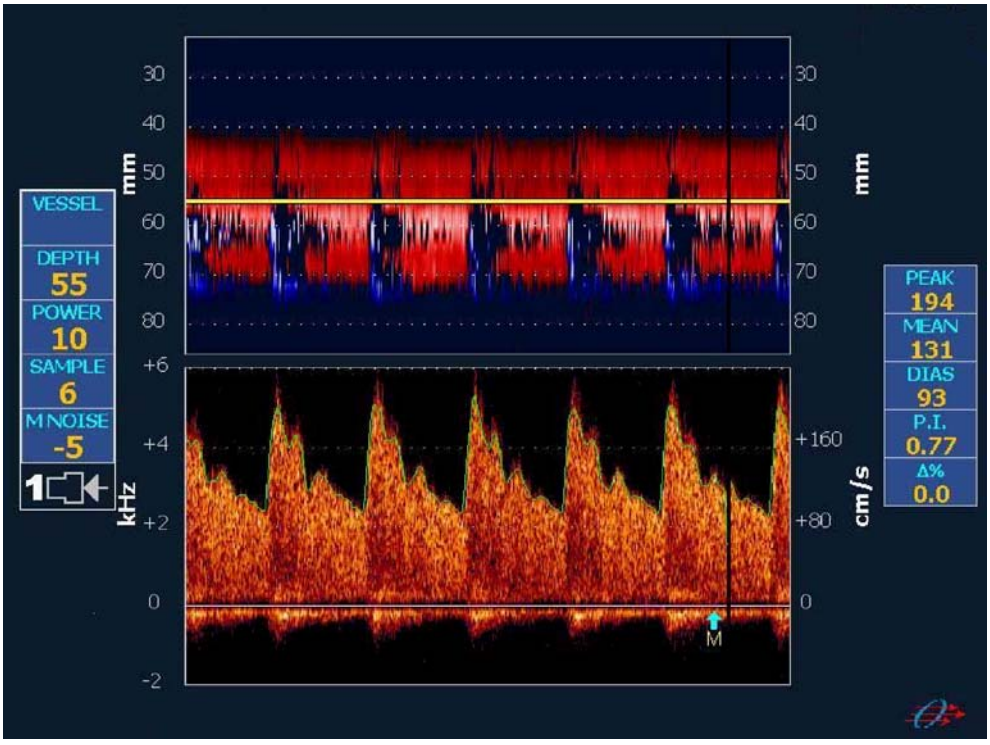

Fig. 3 M mode (*above*) and pulsed-wave Doppler (*below*) illustrating increased mean velocity in MCA consistent with mild to moderate vasospasm

the diameter of the proximal segment of the MCA, ACA and PCA from angiograms. There was an inverse relationship between MCA diameter and MCA FV. Eleven of the 13 MCAs with diameter of 1.5 mm or less exhibited FV greater than 140 cm/s. This was adopted as a useful limit to diagnose marked MCA spasm (50% diameter reduction).

The sensitivity (MCA) ranges from 59% for velocities higher than 100 cm/s to 94% for those above 140 cm/s [38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49]. Vora et al. [50] compared angiographic vasospasm, independently graded by observers, with TCD measurements. Inter-observer agreement regarding angiographic vasospasm was good ($\kappa = 0.86$). Despite significant correlation between mean velocities and the degree of vasospasm the TCD velocity estimates were not dependable. The positive predictive value of an FV of 200 cm/s or greater for moderate/severe angiographic vasospasm was 87% but that of a lower FV was only 50%. The negative predictive value of FV less than 120 cm/s was 94% but that of higher velocities approx. 75%. LR values did not improve the predictive value of TCD monitoring.

In 2001 Lysakowski et al. [51] performed a systematic review comparing TCD with cerebral angiography to diagnose vasospasm following SAH. Meta-analyses as performed with data from 7 of 26 trials. They found that for the MCA sensitivity was 67% (95% CI 48–87%) and specificity 99% (CI 98–100%). For the anterior cerebral artery (3 trials, 171 tests), sensitivity was 42% (CI 11–72%) and specificity 76% (CI 53–100%). Other arteries were tested in only one trial each. The authors concluded that for the MCA TCD is unlikely to indicate spasm when angiography is negative (high specificity) and may be used to identify patients with spasm (high positive predictive value) [51].

Ability of TCD to predict onset of delayed ischaemic deficit

Many of the published reports have attempted to find a correlation between TCD velocity and angiographic evidence of vasospasm. It could be argued that the presence of clinical deficits is more important then radiological vasospasm as only 50% of patients develop DID. Several trials have attempted to compare TCD velocities with clinical evidence of cerebral hypoperfusion [52]. Again, the lack of well-designed trials hampers interpretation of results.

A correlation between TCD velocity and DID has been confirmed by several authors. Sekhar et al. [53] followed 21 patients after SAH, 8 of whom developed neurological deficits. They found a good correlation between TCD velocity in the MCA and ACA and neurological deficits. Similarly, Vora et al. [50] found the specificity of a TCD for diagnosing DID approached 95% (velocity > 200 cm/s). Lam et al. [54] demonstrated that patients with an abnormal result on the transient hyperaemic

response test (see below) after SAH were likely to develop increased FV and DID (Fisher's exact test, $p = 0.0004$).

Other investigators have reported conflicting results. Grosset et al. [55, 56] found that although the highest recorded velocity was greater in the patients who developed DID (186 ± 6 vs. 149 ± 5 cm/s, $p < 0.05$), peak velocity was often recorded only after the onset of neurological deficit. When only the readings made before the onset of DID were considered, there was no significant difference in peak velocity between the groups (157 ± 8 vs. 149 ± 5 cm/s, respectively). The rate of increase in TCD velocity recorded during the first few days after SAH was significantly higher in the patients who later developed DID. They concluded that a rise of more than 50 cm/s in 24 h predicts the onset of DID following SAH.

Klingelhofer et al. [57] failed to identify a consistent relationship between the occurrence and extent of DID and the relative change in mean FV during the clinical course. In contrast, there was a significant correlation between the relative change in the cerebral circulatory resistance index and the occurrence of DID. Mizuno found that only 61% of patients with DID demonstrated increased FV on TCD. Interestingly, subsequent angiograms of the other 39% showed distal vasospasm [58].

Role of TCD for the detection of posterior circulation vasospasm

Only few studies have investigated the role of TCD for evaluation of the posterior circulation. One of the first compared cerebral angiography and conventional hand-held TCD to determine sensitivity and specificity in detection of vertebral and basilar artery vasospasm. TCD was highly specific (100%) for vertebral and basilar artery vasospasm when FV was at least 80 and at least 95 cm/s, respectively [14]. The ability to predict DID, however, is less clear. Clinical studies and those using single photon emission computed tomography confirm that an FV greater than 115 cm/s is required before ischaemia can reliably be predicted [59, 60]. In an attempt to differentiate between hyperaemia and vasospasm Soustiel et al. [61] developed a ratio of intracranial basilar artery (BA) to extracranial vertebral artery velocities, similar to the LR. Comparative analysis between computed-tomography angiography and TCD findings showed a ratio greater than 2 in all patients with BA vasospasm (100% sensitivity) and one less than 2 in patients without BA vasospasm (95% specificity).

Summary

The inconsistency between studies is not surprising and may be attributable to the lack of correlation between angiographic vasospasm and DID, moment to moment variation in velocities [15], potential for probe displacement, spasm distal to the major intracerebral vessels [62], the occurrence of hyperaemia in a subgroup of patients [63] and technical factors including operator variability [64] and difficulty insonating non-MCA vessels. Furthermore, CBF and TCD readings are not always correlated [65, 66, 67]. Spasm may be an episodic phenomenon. This, combined with the fact that intermittent TCD may potentially miss significant peaks or troughs in measurements, creates the potential for false negatives and false positives in the diagnosis of vasospasm. Finally, the theoretical relationship between blood flow, velocity and pressure drop and changes in vessel diameter need to be borne in mind when interpreting alterations in FV to avoid the potential for misinterpretation. With these caveats, TCD measurements can be used to assess the site and severity of vasospasm. Improvements in probe design and fixation together with refinements in signal quality analysis have the potential to lead to greater measurement accuracy.

Traumatic brain injury

A major cause of morbidity and mortality in the Western world is traumatic brain injury (TBI). The pathophysiology and management is complex and poorly understood. The fact that TCD is non-invasive and can be applied at the bedside makes it an ideal tool for investigation of the changing cerebral haemodynamics of the head-injured patient. The technique has been used for the non-invasive assessment of ICP, cerebral autoregulation and vasospasm. Each of these is described in detail below.

Alternations in TCD velocities following TBI

TCD has been used to provide a noninvasive assessment of CBF in TBI (Fig. 4). Published data indicate that FV decreases during the first 48 h after head trauma and subsequently increases between 48–120 h. The delayed increase in velocity may indicate either vasospasm or cerebral hyperaemia [68, 69]. Zurynski et al. [70] measured CBF velocity in 50 severely head-injured patients (Glasgow Coma Scale 8 or less). LR was used to distinguish between hyperaemia and vasospasm. Although the proportion of patients with poor neurological outcome was comparable in the two groups (47% vs. 40%), it was concluded that the ability of TCD to distinguish between the two processes facilitated clinical management. Finally, TCD measurements have demonstrated that low CBF (as indicated by FV < 35 cm/s) is associated with poor neurological outcome [71, 72].

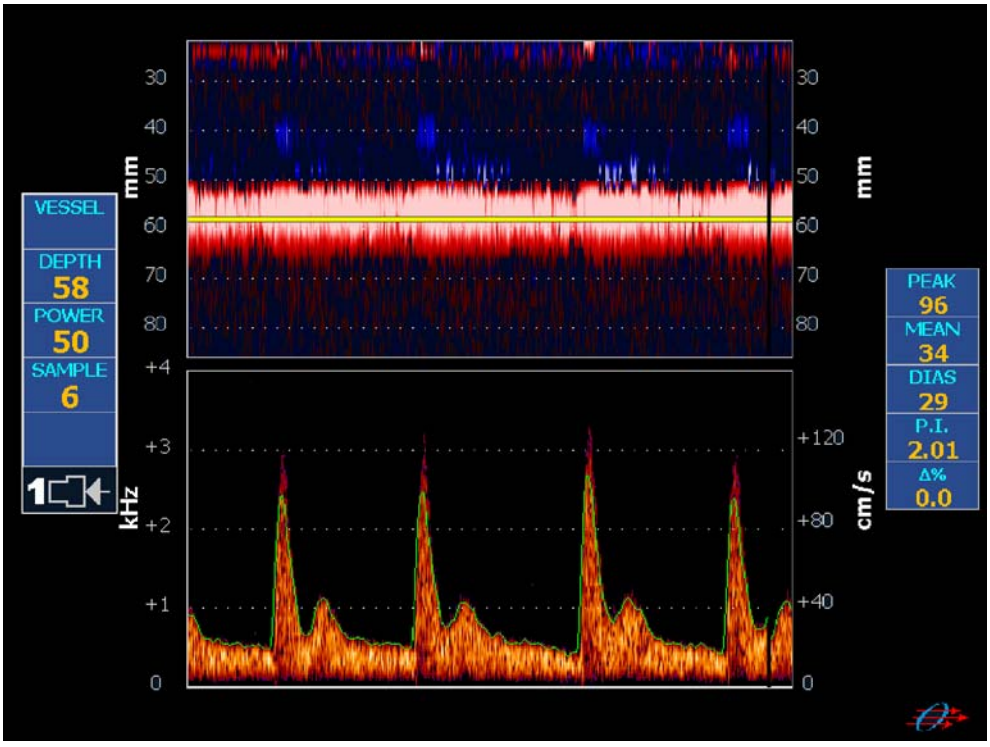

Fig. 4 Spike-wave pattern with raised PI, typical of MCA flow velocity found in patients with intracranial hypertension

Correlation with ICP

The use of TCD as a marker of ICP was initially described by Klingerhofer et al. [73]. In a pilot study changes in ICP were compared with the TCD findings of the MCA. Data from five patients with brain death showed that changes in the ICP influenced the flow patterns considerably. These changes could be recorded quantitatively by means of the PI and the mean FV. Increases in ICP were accompanied by an increase in PI (owing to a decrease in diastolic and mean velocities). The authors subsequently demonstrated an association between ICP and flow patterns in a subgroup of neurosurgical patients with cerebral hypertension [74]. Whilst it is unlikely that TCD will replace invasive ICP monitoring in the near future, it may have a role in situations where the role of invasive monitoring is not clearly established: stroke, paediatric cases, liver failure, minor head injury assessed on accident and emergency wards and preeclampsia [20, 75].

Vasospasm following TBI

Compton and Teddy [76] highlighted the importance of vasospasm as a contributor to poor neurological outcome following head trauma and emphasized the potential role of TCD in the detection of vascular spasm. Using LR values higher than 3 as indicative of spasm, Weber et al. [77] and Martin et al. [78] confirmed the presence of spasm following head injury in 40% of patients. Spasm was not noted in TBI patients without SAH.

Although difficult to diagnose, vasospasm may be identified in the posterior circulation. Soustiel et al. [59, 79] examined the FV of the basilar artery post SAH (both spontaneous and traumatic). BA vasospasm was defined as moderate whenever FV was higher than 60 cm/s and severe when higher than 85 cm/s. BA vasospasm was significantly more common following traumatic SAH (59.7%) than spontaneous SAH (40.3%, $p = 0.041$). Permanent neurological deficit was associated with moderate BA vasospasm while severe vasospasm led to a persistent vegetative state. These findings have been confirmed in several other studies [80, 81, 82].

Assessment of cerebrovascular autoregulation

TCD has been used extensively in the study of autoregulation in the critical care setting. The ability of the cerebral vascular system to constrict and dilate in response to changes in perfusion pressure is termed autoregulation. Cerebral autoregulation can be explained at least partially by a tight coupling between O_2 supply and demand of the brain. Under normal conditions CBF is maintained at a constant flow rate of 50–60 ml per 100 g/min, with 50 ml oxygen being extracted every minute from 700–800 ml

blood [83]. This occurs despite changes in MAP within the range of 60–160 mmHg. Outside this range flow becomes proportional to pressure, potentially leading to episodes of hypo- and hyper-perfusion [84]. Changes in FV in response to fluctuations in blood pressure and arterial carbon dioxide tension have been used as markers of cerebrovascular regulation. Thus autoregulation of the cerebral circulation can be assessed by examining the changes in FV in response to changes in $PaCO_2$ and MAP.

Assessment of autoregulation in response to changes in $PaCO_2$ is termed CO_2 reactivity. In the range of $PaCO_2$ between 20 and 60 mmHg, CBF changes by approx. 3%/mmHg change in $PaCO_2$ [85, 86]. It is important to ensure that hypotension is corrected before testing for CO_2 reactivity. Hypoventilation causes vasodilatation and increased CBF and velocity, while hyperventilation results in vasoconstriction and decreased velocity [87].

Autoregulation in response to changes in MAP can be assessed using a static or a dynamic manoeuvre. In the static technique MCA FV is measured under resting conditions and again following a 20- to 30-mmHg increase in MAP [88]. An index of autoregulation can be calculated as a percentage change in cerebrovascular resistance (MAP/FV) per 1% change in MAP. A value lower than 0.4 suggests impaired autoregulation. The main disadvantage of this technique is the need for pharmacological intervention, which in itself may alter vascular reactivity and has the potential for serious adverse effects. Consequently, less invasive, non-pharmacological, "dynamic" methods have been developed. (a) The classical thigh cuff technique of Aaslid et al. [89] elicits a stepwise drop in AP by applying a thigh pressure cuff, which is then rapidly deflated. Normally, both FV and MAP decrease initially, but FV recovers more quickly. If autoregulation is impaired, FV recovery passively follows the improvement in MAP. (b) Tiecks et al. [90] developed a simpler, less time consuming method using a valsalva maneuver, which evokes a transient decrease in AP and FV. If autoregulation is intact, there is a stronger restoration of FV than of AP during phase II. (c) Giller et al. [91] described the transient hyperaemic response test which evaluates the changes in MCA FV following brief compression of the ipsilateral common carotid artery. The sudden decrease in CPP provokes vasodilatation in the vascular bed distal to the MCA, leading to a transient increase in FV following release of the compression. If autoregulation is lost, FV returns to pretest values without a transient increase.

Loss of autoregulation is common following head injury and is associated with severity of injury and increased mortality [92, 93]. Knowledge of the state of autoregulation may permit individualization of therapy [94, 95, 96, 97]. The process is rapid, but not instantaneous, allowing for assessment using both static and dynamic tests. Although CBF is not directly measured by TCD, changes in velocity are correlated with flow if the vessels cross-sectional area remains constant.

Summary

Despite initial enthusiasm for the technique, to date there have been no well-designed studies demonstrating a positive outcome effect from the use of TCD in head injury. The main role of TCD in neurotrauma appears to be in its ability to provide information on cerebrovascular reactivity and CBF. Whilst the PI may be used as a surrogate for ICP, it is unlikely to replace invasive pressure monitoring. Its role in the identification of vasospasm in the setting of traumatic SAH needs further evaluation. TCD may also have a role as an adjunct in the diagnosis of brain death.

Brain death

The law in many countries requires the demonstration of loss of cerebral function (via electroencephalography) and/or CBF before brain death can be confirmed [98]. Angiography is considered the gold standard but is laborious and logistically complicated, as the patient must be moved from the ICU environment for the study to be performed.

Over the past two decades case reports detailing the use of TCD to confirm cerebral circulatory arrest and by inference brain death have emerged [99, 100]. As an acoustic window is absent in 8% of patients, it is necessary to have demonstrated cerebral perfusion on TCD prior to the onset of brain death. With increasing ICP, TCD waveforms exhibit characteristic high-resistance profiles, first with low, then zero, and then reversed diastolic FV [101] (Fig. 5). The flow patterns depend on the relationship between ICP and CPP and are correlated with the level of cerebral circulatory arrest as demonstrated by angiography. As CPP approaches zero, three patterns of TCD waveforms are observed: oscillating flow, small systolic spikes and no signal [101, 102]. It is not clear which pattern is the most sensitive or specific for diagnosing cerebral circulatory arrest. Furthermore, studies differ in their description of "TCD brain death" making comparisons difficult. In the ICU setting the most commonly insonated artery is the MCA. The posterior circulation should also be insonated, especially in patients with cerebellar pathology. There are additionally reports of Doppler studies of the ophthalmic arteries correlating with signs of brain death [103].

Although the sensitivity of TCD for the diagnosis of brain death is 91.2–100%, the specificity is reported to be virtually 100% [99]. There have been several case reports of patients with demonstrable CBF on TCD who were clinically brain dead. In these cases the pathology was limited to the cerebellum or brainstem leaving blood flow in the anterior cerebral circulation relatively intact. For this reason it is important that patients show clinical signs of brain death before performing TCD.

TCD is especially useful in patients who are known to have received sedative drugs. Hadani et al. [104] reported that 31.4% of comatose patients had received sedation and

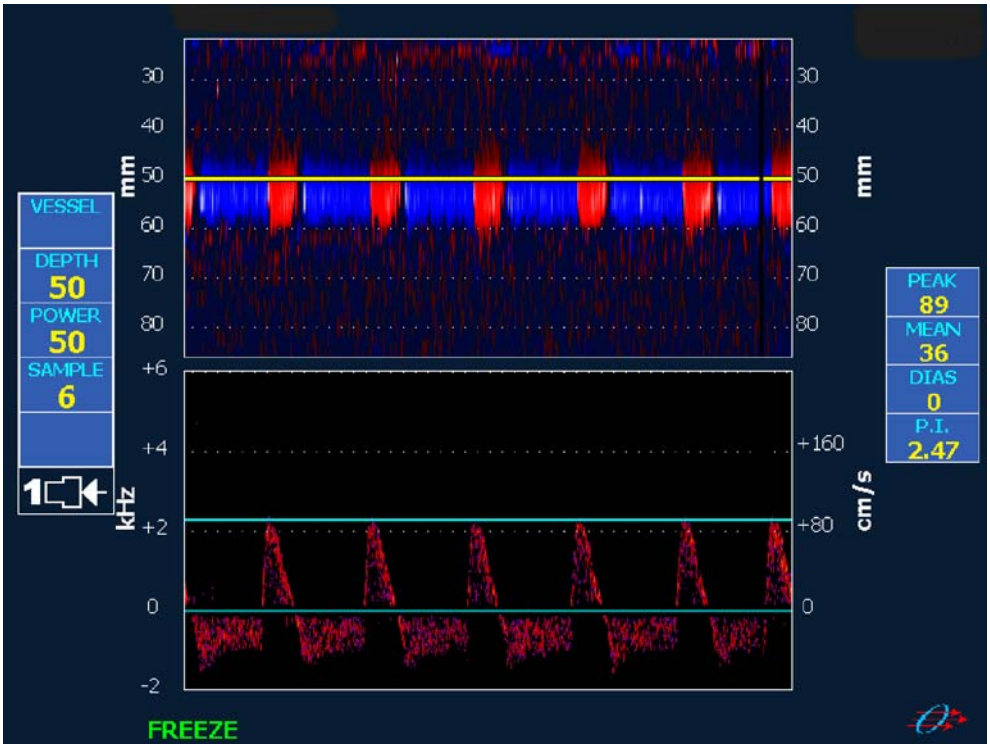

Fig. 5 MCA TCD pattern demonstrating an increasing ICP and decreasing CPP associated with progression to brain death. Note reversal of diastolic flow once ICP is greater than diastolic blood pressure. This can be seen as *intermittent blue* (flow away from probe) on M Mode and negative wave deflection on Doppler

could therefore not be declared brain dead. TCD confirmed cessation of CBF. Germany now includes TCD in their brain death guidelines [105].

Transcranial Doppler of the cerebral veins and sinuses

In 1982 Aaslid et al. [2] described a technique for insonating the straight cerebral sinus using a transorbital approach. Subsequently, transcranial colour-coded duplex sonography has been used to define a range of normal values of both cerebral veins and sinuses (Table 3) [106]. Unfortunately, there have been few studies on the possible applications of venous transcranial ultrasonography in the ICU. One possible use is the non-invasive assessment of ICP. Schoser et al. [107] demonstrated a linear relationship between the measured ICP and FV of the straight sinus. The degree of midline shift can also be assessed, as this produces a distortion in venous flow. Another potential application is cerebrovascular monitoring following SAH. Mursch et al. [108] found a good correlation between velocities in the basal vein of Rosenthal and CBF following SAH.

Other developments in TCD applications

Advances in technology have stimulated a renewed interest in the use of non-invasive, portable and easy to use tools for the monitoring of cerebral haemodynamics in a variety of disorders. Three-dimensional power Doppler ultrasonography imaging provides rapid, noninvasive visualization of ruptured intracranial aneurysms, including their relationship to other vascular structures [109].

Table 3 Normal values of peak systolic (*PSV*) and end-diastolic (EDV) flow velocities of the intracranial veins and sinuses based on transcranial colour-coded sonography (*dMCV* deep middle cerebral veins, *BVR* basal veins of Rosenthal, *GV* great vein of Galen, *ICV* internal cerebral veins, *SRS* straight sinus, *TS* transverse sinus, *SSS* superior sagittal sinus)

Vein	Window	Depth (cm)	PSV (cm/s)	EDV (cm/s)
dMCV	Temporal	5.2 ± 0.5	8.7 ± 2.9	5.8 ± 1.9
BVR	Temporal	6.2 ± 0.4	12.2 ± 3.8	8.7 ± 2.8
ICV	Temporal	7.4 ± 0.5	7.2 ± 1.7	4.9 ± 1.1
GV	Temporal	7.4 ± 0.5	11.9 ± 3.6	7.7 ± 2.8
SRS	Temporal	9.3 ± 0.6	12.1 ± 4.7	8.6 ± 3.7
TS	Temporal	11.5 ± 0.9	14.0 ± 5.9	9.7 ± 4.8
SSS	Temporal	10.6 ± 2.0	9.8 ± 3.6	6.1 ± 2.5

Contrast agents such as Levovist, Sonovue and Echovist are being employed to provide better visualization of the microcirculation. These are largely gaseous microbubbles stabilized in a surrounding shell. Insonation of these contrast agents at a fundamental frequency leads to minimal tissue resonance, facilitating improved visualization of the microcirculation. They appear to have a high sensitivity and specificity in the detection of intracranial stenosis when compared to magnetic resonance angiography [110]. Ultrasound probes attached to stethoscopes (Neurodop) allow the rapid assessment of MCA velocities in the ED and may prove useful in the management of stroke patients [111]. Larsen et al. [112] have investigated CBF, FV and autoregulation following fulminant hepatic failure and during liver transplantation. They suggested that the CBF is not autoregulated in patients with hepatic failure and therefore CBF should be "clamped" within the normal physiological range by manipulation of arterial blood pressure in order to avoid cerebral hypoxia and/or hypertensive induced cerebral oedema. Functional transcranial Doppler is being developed as a tool in psycho-physiological research [113], although immediate application in intensive care is not available. Ultrasound has also been reported to have therapeutic benefits through enhancement of liposome-mediated gene transfer to eucaryotic cells in culture [114]. These effects are thought to be mediated by cavitation. As in the case of functional Doppler, this modality has no routine use in clinical intensive care practice.

The future of TCD in intensive care

Whilst class I data exist for the role of TCD in the management of patients with sickle cell disease [115], robust evidence for its usefulness in the critically ill is lacking. Although evidence of its diagnostic capabilities in a variety of conditions is emerging, its current application in intensive care is confined largely to the management of patients with SAH, assessment of brain death and monitoring of cerebral haemodynamics in neurotrauma.

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