Transcranial Doppler (TCD) Ultrasonography and its Clinical Application-A Review and Update

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Abstract

Transcranial Doppler (TCD) Ultrasonography is a bedside, non-invasive duplex study of intracranial blood flow dynamic through some selected region or window in the cranial region. TCD provides information about the physiology of blood flow in the basal intracranial major arteries by measuring flow velocity and pulsality in different segment of these arteries. The physiologic data obtained from the cerebrovascular hemodynamic are complimentary to anatomical data obtained from various imaging techniques and it can be used as bedside monitor to assess the cerebrovascular changes in response to any intervention. Common application of TCD includes detection of vasospasm after subarachnoid haemorrhage, vasodclusion in sick cell disease, cerebral strokes, intracranial pressure monitoring, intraoperatively monitoring to detect micro-embolism, early detection of brain death and cerebral auto regulatory testing. The review focus on basic principles of TCD, scanning techniques and described application of TCD in some of the common clinical conditions.

Keywords: Transcranial Doppler Ultrasonography; Cerebral blood flow; Cerebral vasospasm; Sick cell disease; Intracranial pressure; Brain death; Cerebral auto regulation

Abbreviations: TCD: Transcranial Doppler; CBF: cerebral blood flow; PSV: peak systolic Velocities; EDV: End Diastolic Velocities; PI: Pulsatility Index; RI: Resistive Index; MCA: middle cerebral artery; ACA: Anterior cerebral Artery; PCA: Posterior Cerebral Artery; BA: Basilar Artery; VA: Vertebral Artery; MAP: Mean Arterial Pressure; MFV: Mean Flow Velocity; ICP: Intracranial Pressure; NPV: Negative Predictive value

Introduction

Transcranial Doppler (TCD) Ultrasonography is a non-invasive technique that utilised a pulsed low-frequency ultrasonic transducer of low frequency through some selected region (window) in the cranial region to enable recording to flow velocity pattern in intracranial arteries. Unlike the cerebral angiography which provides an anatomical configuration of both extra and intracranial arteries and their smaller branches, TCD provides information about the physiology of blood flow in the basal intracranial major arteries by measuring flow velocity and pulsality in different segment of these arteries [1,2]. TCD being relatively inexpensive, non-invasive, reputable, portability and provides real time information that makes it more practical and convenience as bedside monitoring in intensive care setting for cerebral blood flow (CBF) velocity [3-5].

Aaslid et al. [6] in the year 1982 first demonstrated the technique of using pulsed Doppler ultrasound (without imaging facility) through transtemporal approach to measure the cerebral blood flow velocities [6]. The technique they used was non-duplex (non-imaging) or blind as there was no direct grey scale sonographic visualisation of cerebral arteries, the identity of the vessel being interrogated was determined by standard criteria that included transducer orientation, depth of the sample volume and direction of blood flow. This technique is still in use by many clinicians, however, inability to direct visualize target vessels and to perform angle correction, may have led to errors in the velocities recorded with this technique. The Power-motion mode Doppler or M-mode Doppler was described by Mark Moehring [7] in 2002 with 33 sampling gates to detect cerebral blood flow and cerebral embolism [7]. Modern TCD involves use of spectral Doppler and colour Doppler in addition to grey-scale tissue imaging that allows direct visualization of the major intra cranial arteries, allowing quick, accurate identification of arteries and their flow velocity dynamics.
Basic Principle

TCD Ultrasonography, like all Doppler imaging studies, is based on two main principles; the Doppler Effect and the Bernoulli principle. Sound wave with certain frequency when strikes a moving object, the frequency of the reflected sound wave is changes. The differences in the frequency between emitted and reflected waves is called “Doppler shift frequency” that is directly proportional to the speed of the moving object (blood flow in TCD). If the flow is towards the probe, results in shift to a higher frequency or positive Doppler shift and if the flow is away from the probe results in Doppler shift to lower frequency or negative Doppler shift. Since blood flow within a vessel is laminar, the Doppler signal obtained actually represents a spectral display of mixture of different Doppler shift from individual red blood cells [4].

The relationship between flow velocity and Doppler shift frequency is express by following formula

\[
\text{Reflector speed (cm/s)} = \frac{(\text{Doppler Shift}) \times \text{propagation speed}}{2 \times \text{Incident frequency} \times \cos (\theta)}
\]

The propagation speed a sound wave in a particular medium, \( \theta \) is the angle of insonation relative to the direction of the blood vessel. The larger the angle of insonation, the larger is the cosine of the angle, and greater error in the measurement. If the angle is 0, (angle of insonation parallel to flow). We achieve the most accurate flow measurement since the cosine of 0 is 1. It is important to keep the angle below 30 degrees to keep the error below 15% (Figure 1).

Figure 1: Diagram shows the Doppler effect. Sound waves emitted at a specific frequency \( f_0 \) are reflected off moving red blood cells and back to the transducer at a higher or lower frequency \( f_r \). The difference in frequencies, known as the Doppler shift, can be used to calculate the blood flow velocity \( V \) and direction. \( \theta \) = angle between the incident ultrasound beam and the direction of blood flow.

The Bernoulli principle described the flow in terms of velocity and pressure of liquid (blood) through different size of conduit (vessels). Blood flow velocity increases and pressure decreases when blood flow from a greater to lesser diameter (vasospasm), this is to allow the same volume of blood pass through narrow area. The changes in blood velocity (detection of vasospasm) can be estimated using Doppler Effect and Doppler equation (Figure 2).

Figure 2: Diagram of the Bernoulli principle shows that as fluid flows from a conduit or vessel of greater diameter to one of lesser diameter, the velocity of flow increases and the pressure decreases to allow the same volume of fluid to pass through the narrower area.

TCD relies on pulse wave Doppler to image a particular vessel and a received echo generates an electrical impulse which is processed electronically to produce a spectral waveform [8,9]. A spectral Doppler waveform is visual display of flow-velocities within a specific are of blood vessels as a time velocity curve. Spectral analysis can thus be use to estimate not only the blood flow velocity; it can also used to calculate the peak systolic (PSV) and end diastolic (EDV) velocities, systolic upstroke or acceleration time, pulsatility index (PI), resistive index (RI) and time averaged mean maximum velocity (V mean) (Figure 3). TCD devices are equipped with larger sample volume unlike the normal Pulse Wave Doppler (PWD) for other uses; this is to obtain better quality of signal in noisy background also. Standard TCD is recorded bilaterally using PWD for at least 10 cardiac cycles [10].
Image Technique

The TCD Ultrasonography examination is performed by using phase array probe of 1-2 MHz. The higher frequency waves have lower penetration and not able to penetrate the through the skull bone in adults and hence are not useful for intracranial scanning [8,9]. Based on anatomical location of the major cerebral arteries and ease of ultra sound penetration into brain though thinner region of skull has been identified, termed as acoustic window [8,9].

Four Acoustic Windows Are Used For TCD

Transtemporal, transformational or sub occipital, Transorbital and submandibular (retromandibular). Each window specifically target particular portion of major branch of the circle of Willis, which are first optimally scan using grey scale and colour flow imaging; once a particular vessel is identified, spectral waveform are obtained using pulse wave Doppler [3,8-10]. The most commonly used acoustic window is transtemporal window, located above the zygomatic ridge between the lateral canthus of the eye and auricular pinnia, through this window all three major arteries (anterior, middle and posterior cerebral arteries) forming the circle of Willis as well as terminal portion of Internal carotid artery can be insonated (Figure 4). once probe is placed in the temporal window, identification of sphenoid bone, through the butterfly wing sign guide the visualization of the middle cerebral artery (MCA) in almost
all patients which usually lies at depth of 50-65mm indicated by red colour signal as flow is towards the probe, with fine adjustment and following the flow pattern, the branching of MCA can be identified. The internal carotid artery (ICA) bifurcation observed at about 55-70mm in adults and is represented by bidirectional flow (red and blue in colour Doppler), the Anterior cerebral artery (ACA) flow is away from the probe (blue) (Figure 4).

Once signal from MCA and ACA are obtained, the ultrasound probe is slowly oriented posteriorly by 10-30 degrees, initially there will be a flow gap before signals from the posterior cerebral artery (PCA) is obtained at 55-70mm. Two segment of PCA are obtained, P1 represented by flow towards the probe and P2 away from the probe.

Transformational or sub occipital approach involve placing the transducer in sub occipital region in a flex neck, in mid line below the occipital, medial to the mastoid process and the probe is angled or tilted towards the bridge of the nose or contra lateral eye to insonate portion of the vertebral artery (VA) at a depth of 50-75mm (flow away from the probe) and further upward and medial tilting of probe is done to obtained from the basilar artery (BA) at a depth of 75-110mm (Figure 5).

Figure 5: Color Doppler flow image obtained with a Transformational or sub occipital window shows the vessels of the posterior cerebral circulation.

Figure 6: Submandibular and Transorbital windows.
Transorbital approach involves placing Ultrasonography probe gently on the closed eye lid to visualize the ophthalmic artery and the cavernous portion of the internal carotid artery (carotid siphon). The probe is angled slightly medially and upward, at around 60 mm ophthalmic artery can be traced followed by trace from the carotid siphon. Sub mandibular window is at just below the angle of jaw and can be used to locate the distal extra cranial portion of internal carotid artery in the neck (Figure 6).

Target artery is identified depending on the appropriate acoustic window, probe orientation and angle, depth of insonation and direction of flow, in difficult scenario when it is not possible to differentiate the anterior from posterior artery, dynamic maneuvers such as direct carotid compression or vibration and resulting waveform changes are recorded [3,9].

**TCD Indices**

Peak Systolic Velocity (PSV): The maximum value of flow velocity in systole, at the apex of the waveform.

End Systolic Velocity (EDV): The velocity measured at end diastole, usually at the lowest point before a new waveform begins. The central parameter in TCD is the mean flow velocity (MFV) which can be calculated similar to that of mean arterial pressure (MAP), the MFV is equal to 1/3rd PSV + 2/3rd EDV. (MFV= {PSV+EDV x 2}/3). The MFV can be influenced by number of physiological factors [11-13] (Table1).

**Table 1: Physiological Factors Influencing MFV.**

<table>
<thead>
<tr>
<th>Physiologic Variable</th>
<th>Change in MFV</th>
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<tbody>
<tr>
<td>Age</td>
<td>Increases up to 6-10 years of age then decreases</td>
</tr>
<tr>
<td>Sex</td>
<td>Higher MFV in women than men</td>
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<tr>
<td>Pregnancy</td>
<td>Decreased in the 3rd trimester</td>
</tr>
<tr>
<td>PCO2</td>
<td>Increases with increasing PCO2</td>
</tr>
<tr>
<td>Mean arterial Pressure (MAP)</td>
<td>Increases with increasing MAP (CBF Auto regulates between CPP 50-150 mmHg)</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>Increases with decreasing Haematocrit</td>
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</table>

Common pathological factors increasing MFV are vasospasm, stenosis, hyper dynamic flow, whereas, hypotension, decrease in cerebral blood flow, intracranial pressure or brain stem death [11] other important TCD indices are:

**Gosling’s pulsatility index (PI)**

This is the most commonly used TCD parameter to determine the flow resistance. PI is the measure of pulsatility of blood flow that reflects the resistance to blood flow. It is the difference between systold and diastolic flow velocity divided by mean velocity. It is calculated as PI= (PSV-EDV)/MFV. Normal value=0.5-1.19. Downstream obstruction will increase the PI and proximal obstruction or stenosis may decrease the PI due to down stream vasodilatation [14,15]. Also it is affected by change in Intra Cranial Pressure (ICP) in a linear way and a progressive rise in PI may reflect rise in ICP [16,17]. Patients with Arterio-Venous (A-V) malformation will have reduced PI as the resistance to flow suddenly reduced due to distal venous flow [18].

**Pourcelot resistivity index (RI)**

It is similar to pulsatility index. It measures the resistance to blood flow distal to the site of measurement. It is calculated as RI= (PSV-EDV)/PSV; value greater than 0.8 indicates increased in downstream resistance [11].

**Lindegaard ratio (LR)**

It’s a ration of mean flow velocity in intracranial to extra cranial carotid artery and calculated as MFV in Middle cerebral artery/MFV in extra cranial internal carotid artery [19]. The LR differentiates between hyper dynamic flows from vasospasm. LR more than 3 indicates cerebral vasospasm. A high LR ratio indicates increased in intracranial flow due to vasospasm and abnormally low LR indicates hyper dynamic flows like in A-V malformation [20]. A modified LR ratio for intracranial basilar and extra cranial vertebral artery can also be cam also be used to calculate vasospasm in posterior circulation [21].

**Micro embolic signal (MES) detection**

TCD a useful monitor intraoperatively for carotid and other cardiac surgery where there is high risk of micro embolism [22,23].
Abnormal spectrum waveforms

Delayed systolic flow acceleration or flattened systolic upstroke and slow diastolic deceleration with end diastolic velocity (EDV) above 50% of peak systolic velocity (PSV) is hallmark of stenosis proximal to the site of PWD this is known as blunted flow, and is clinical application of TCD

<table>
<thead>
<tr>
<th>Cerebro-Vascular Ischemic Diseases</th>
<th>Perioperative/Periprocedural Monitoring</th>
<th>Neuromonitoring in ICU</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sickle cell disease</td>
<td>Cerebral thrombolysis in acute stroke</td>
<td>Vasospasm after subarachnoid haemorrhage</td>
<td>Pharmacologica vasomotor testing</td>
</tr>
<tr>
<td>Right to left cardiac shunts</td>
<td>Carotid endarterectomy</td>
<td>Raised intracranial pressure</td>
<td>Cerebral pressure auto regulation</td>
</tr>
<tr>
<td>Intra and extra-cranial arterial steno-occlusive disease</td>
<td>Carotid angioplasty and stenting</td>
<td>Head injury</td>
<td>Liver failure/Hepatic encephalopathy</td>
</tr>
<tr>
<td>Arteriovenous malformations and fistulas</td>
<td>cardiac surgeries to detect microemboli</td>
<td>Cerebral circulatory arrest and brain death</td>
<td>Preeclampsia</td>
</tr>
</tbody>
</table>

TCD was initially used to diagnose vasospasm following subarachnoids haemorrhage. However, a clinical use of TCD has expanded greatly over the decades and it has emerged as bedside, non-invasive tool for evaluating cerebral artery patency, detection of stenosis, embolism, flow pattern and even as alternative monitoring of ICP. Common clinical applications of TCD can be summarised as categorical groups (Table 2).

Monitoring of vasospasm in subarachnoid haemorrhage (SAH)

TCD was initially invented for monitoring of cerebral vasospasm after SAH [6,7]. The basis of using TCD in vasospasm is on Bournellis principle, the narrowing of vessel will lead to increase in velocity of blood flow, even though absolute flow decreased. TCD is a reliable, cost effective tool for monitoring of vasospasm after SAH delayed cerebral vasospasm is one of the common complication after SAH, can occur in up to 70% between 4-17 days, which can leads to delayed ischemic deficit in up 25% patients [24-26]. There are reports of early vasospasm within 48 hours in up to 13% cases, [27-32] and much delayed vasospasm even after 20 days; morbidity and mortality are considered to increase significantly, longer the period of vasospasm [33]. Use of TCD can be used to early detection of even asymptomatic vasospasm, follow progression of vasospasm and can be used to monitor the effect of treatment or intervention for vasospasm [34-39].

Suggested protocol for TCD in SAH by Sharma et al [38]:

a. First baseline TCD as soon as possible after the diagnosis of SAH. Flow velocity to be obtained from both extra cranial and intracranial artery to calculate the LR index.

b. Daily or more frequently if needed evaluation by TCD for early detection of vasospasm.

c. Standard diagnostic criteria to be used for diagnosis of Vasospasm (Table 2).

d. If TCD suggested of vasospasm, to initiate treatment for vasospasm and TCD re-evaluation every 6-8 hours.

e. Information regarding ICP if available should be taken into account during interpretation of TCD.

f. In doubtful finding, other diagnostic modality (imaging) should be employed.

TCD in comparison to angiography has good sensitivity and specificity in diagnosis vasospasm for both MCA and VA [35,40,41]. Mean flow velocity (MFV) of MCA greater than 120 cm/sec has 99% specificity and 67% sensitivity to identify angiographic vasospasm of 25% or more [41]. The positive predictive value (PPV) increases to 98% when MFV exceed more than 200 cm/sec whereas, when the MFV less than 12 cm/sec has 94% negative predictive value (NPV) [42]. Therefore, MFV of more than 200 cm/s or less than 120 cm/sec could predict both present and absence of MCA vasospasm, respectively. Unlike the sensitivity and specificity of even in mild vasospasm of MCA, TCD is little weaker in detecting less than 50% narrowing in VA and BA [35,40,43,44].

Similarly, ACA and PCA vasospasm has lower specificity and sensitivity in mild to moderate vasospasm unlike the MCA vasospasm [45]. It is daily changes in MFV that is more important than the absolute value; an increase in MFV is highly predictive of vasospasm. MFV rise of 50cm/sec or more within 24 hours or MFV increases of more than 65cm/s per day from day 3-7 indicate development of vasospasm and high risk for delayed cerebral ischemia [46,47]. Though the TCD is a valid diagnostic tool to identify and to monitor the development of intra cerebral vasospasm after SAH. The interpretation of TCD finding should be correlated with clinical assessment and other diagnostic tools like computed angiography should be used for diagnosis of vasospasm after SAH instead of the single independent test [47,48].

Acute ischemic/embolic stroke

TCD can accurately identify acute occlusions of intracranial arteries with high, specificity, sensitivity, PPV, and NPV of greater due to compensatory vasodilatation distal to the stenosis (Figure 7). Patients with focal intracerebral stenosis/vasospasm- there will be focal flow acceleration, with increasing stenosis; the increased in the flow creates flow turbulence, represented by bruit, which is seen as symmetrical artefact on either side of baseline.
than 90% for MCA and 70-90% for ICA siphon, VA and BA [49]. TCD has been compared with Magnetic resonance angiography (MRA) and Computed tomography angiography (CTA) in early evaluation in acute ischemic strokes. It has been used to assess steno-occlusive pathology of terminal ICA, ICA siphon and MCA. TCD is almost 100% specific and 93% sensitive for identifying the MCA ischemia, whereas MRA had 74% specificity and only 46% sensitivity in the assessment of Intracerebral arteries. Moreover, TCD can be used in emergency department as bed side tool and provide real time information about cerebral blood flow (CBF) [50-52].

In addition to diagnostic tool, TCD has more prognostic value in strokes. A complete arterial occlusion at presentation predicted worse neurologic outcome, disability and death after 90 days,[53,54] a normal TCD finding predicted early neurological improvement [47,55]. Unlike other imaging modality, the advantages of TCD are that it can be used serially to detect any cerebral hemodynamic changes that would otherwise go undetected by a single MRA, CTA studies [56].

TCD is also useful to assess the hemodynamic changes before and after thrombolysis; recanalisation within 6 hours of symptoms onset or within 30 min of thrombolysis is associated with marked clinical improvement and functional independence at 3 month [57,58]. TCD can also be useful tool to detect early reocclusion after thrombolysis.

Table 3: STOP classification for risk stratification and treatment strategy [64].

<table>
<thead>
<tr>
<th>Group</th>
<th>TAMM Velocity</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;170 cm/s</td>
<td>A repeat assessment is indicated</td>
</tr>
<tr>
<td>Conditional</td>
<td>170-200 cm/s in the MCA and/or terminal ICA</td>
<td>In children with no previous records, a repeat TCD is planned in about 2 weeks</td>
</tr>
<tr>
<td>Abnormal</td>
<td>&gt;200 cm/s in the MCA and/or terminal ICA</td>
<td>Urgent blood transfusion is arranged</td>
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</table>

Traumatic brain injury (TBI) and raised ICP

TBI have spectra of effects on brain and cerebral circulation, immediately after trauma, there may be hypo perfusion (day 0) followed by hyperaemia (day 1-3), there may be delayed vasospasm and raised ICP after the initial phase is over [65]. TCD as a non-invasive tool can be used to early detection of cerebral hemodynamic changes, it also provide long term prognostic information. TCD derived pulsatility index (PI) provides useful information about ICP and CPP, avoiding complications of invasive monitoring [16,17,66] Recently Wakerley et al. [67], conducted a study to define the relationship of PI and ICP, they performed TCD measurement and simultaneously Lumbar puncture for ICP measurement. TCD-PI has acceptable accuracy in differentiating patients with ICP more than 20cm of cerebrospinal fluid (CSF). Serial measurement over short period of time are reliable than single measurement [67]. There is no standardisation technique or formula for absolutely quantifying the ICP/ CPP by TCD method, hence at present, TCD is reserved for assessing serial data, rather than absolute value.

TCD monitoring for spontaneous emboli

Emboli from carotid plaque or from cardiac origin (left atrial thrombus or right to Left shunt) can produce cerebral ischemia by blocking regional perfusion. Extended monitoring of intracranial artery distal to embolic origin site can detect spontaneous microemboli called Micro-embolic signals (MES).

The International Cerebral Hemodynamic Society described MES as [38]

a. Random occurrence during the cardiac cycle.

b. Brief duration (usually <0.1 s).

c. High intensity (>3 dB over background).

d. Primarily unidirectional signal (if fast Fourier transform is used).

e. Audible component (chirp, whistle, or pop).

Patients with history of cerebrovascular ischemia or high grade carotid stenosis can also undergo TCD monitoring for MES [68-70]. MES can also be used to assess the treatment effectiveness after initiating anti platelet drug therapy in carotid stenosis [71,72].

Right to left (R-L) shunt detection

Patent foramen ovale can be present in approximately 25% of general population and these patients are at risk of paradoxical
Cerebral auto regulation refers to the maintenance of cerebral blood flow (CBF) despite changes in cerebral perfusion pressure over the range of 50-150mm/hg [82-84]. A pressure reactivity index Prx and CBF related index has been introduced to assess the cerebral auto regulation [85] but none of the index has been considered as gold standard [86]. Changes in MFV in MCA is used as surrogate for changes in CBF. Many different non-pharmacologic techniques such as direct carotid artery compression, Valsalva manoeuvre, application of PEEP, head up tilting, negative pressure to lower body portion etc were used to induce pressure changes [87-90].

The TCD assessment of cerebral auto regulation is still an area of clinical research given the high temporal resolution, convenience and non-invasiveness of the technique. Significant auto regulatory impairment in TBI and strokes are common and are associated with poor neurologic outcome. However, the role of auto regulatory assessment in carotid stenosis, syncope or extra cranial pathology is less clear.

**Conclusion**

TCD being non-invasive, portability and provide real time information and high temporal resolution have promoted its use as bedside neuro monitoring tool. Majority of its use are early detection of impaired cerebral flow dynamic and it helped in initiation of preventive measures in SAH, SCD, TBI and Strokes or even preparation of organ retrieval in impending brain death. Advanced application of TCD includes evaluating various mechanism of cerebral ischemia. TCD helps in planning and monitoring the cerebral hemodynamic, effectiveness of therapy as well as idi in establishing the prognosis. The main limitation of TCD is high operator dependency and it requires some technical expertise and training to standardise its application.

**References**

7. The modern Power-motion mode Doppler or M-mode Doppler was described by Mark Moehring in 2002 with 33 sampling gates to detect cerebral blood flow and cerebral embolism p. 7.


