Transcranial Doppler Ultrasound Applications in Neurology and Neurocritical Care: Literature Review

Aplicações do Ultrassom Doppler Transcraniano na Neurologia e Terapia Intensiva Neurológica: Revisão da Literatura

Carolina Rouanet Cavalcanti de Albuquerque[1], Ingrid Pereira Marques[2], Daniel Paes de Almeida dos Santos[3], Bruno Castelo Branco Rodrigues[4], Rita de Cássia Leite Fernandes[5]

[1]M.D., PhD.,Neurologista, Neurointensivista. Serviço de Neurologia Profº Sérgio Novis, Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro. Secretária do Departamento Científico de Neurossonologia da Academia Brasileira de Neurologia. Especialização em Neurologia Vascular e Neurointensivismo pela Universidade Federal de São Paulo, UNIFESP. Intensivista pela Associação de Medicina Intensiva Brasileira (AMIB)

[2]M.D. Neurologista pela Universidade Federal do Rio de Janeiro, Serviço de Neurologia Profº Sérgio Novis, Hospital Universitário Clementino Fraga Filho; Especialização em Neurologia Vascular e Neurointensivismo pela Universidade Federal de São Paulo, UNIFESP; Neurossonologista pela Academia Brasileira de Neurologia. Mestranda do Instituto D'Or de Ensino e Pesquisa.

[3]Membro titular da Academia Brasileira de Neurologia. Membro Titular do European Board of Neurology. Rotina da Neurointensiva do Hsopital Copa Star

[4]M.D., MSc., Neurologista, Serviço de Neurologia Prof. Sérgio Novis, Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro. Médico Rotina na Unidade Neurointensiva do Hospital Copa Star. Intensivista pela Associação de Medicina Intensiva Brasileira (AMIB)

[5]M.D., PhD., Neurologista, Serviço de Neurologia Prof. Sérgio Novis, Hospital Universitário Clementino Fraga Filho,Universidade Federal do Rio de Janeiro. Professora Adjunta II do Deptº Clínica Médica da Faculdade de Medicina-UFRJ; Vice-coordenadora do Deptº Científico de Neurossonologia da Academia Brasileira de Neurologia; Membro do "Council of Nations of the European Society of Neurosonology and Cerebral Hemodynamics"

ABSTRACT

Background: Transcranial Doppler (TCD) has gained increasing evidence in the field of Neurology and Neurointensive Care. It provides real time evidence of cerebral blood flow (CBF) estimated through blood flow velocities (BFV), pulsatility index (PI) and spectral waveform analysis. Its most established applications are the detection of vasospasm in subarachnoid hemorrhage (SAH), stroke prevention in children with sickle cell disease and as a complementary method in brain death diagnosis. TCD can also be used for stroke work-up in detection of cardiac or extra cardiac right-to-left shunts, evaluation of microemboli, intracranial stenosis, vasoreactivity, and as a non-invasive tool of intracranial pressure (ICP) monitoring and cerebral autorregulation.
Objectives: We aimed to review the most recent evidence regarding TCD principles, technique and applications, its main advantages and limitations.
Methods: We performed a comprehensive review in literature databases regarding TCD, cerebrovascular diseases work-up and management, besides aids in neurocritical management.
Results: TCD has a strong well-established role in stroke prevention in children with sickle cell disease and in management of vasospasm/delayed cerebral ischemia in SAH. Other indications such as stroke and hemodynamics understanding in critically ill patients have been gaining importance and popularity.
Conclusions: TCD is a useful, safe and feasible tool that can be used in both in and out of hospital scenarios. It is of utmost importance for stroke work-up and prevention. It is gaining increasing evidence as a non-invasive method of estimating intracranial pressure and autorregulation, besides being consecrated as a complementary tool in brain death.

Keywords: Transcranial doppler, ultrasound, subarachnoid hemorrhage, sickle cell disease, stroke, brain death

RESUMO

Fundamento: O Doppler Transcraniano (DTC) vem ganhando importância crescente no campo da neurologia e da terapia intensiva. Ele fornece evidência em tempo real do fluxo sanguíneo cerebral (FSC) através das velocidades de fluxo sanguíneo (VFS), índices de pulsatilidade (IP) e análise das ondas espectrais. Suas aplicações mais populares são para detecção de vasoespasmo na hemorragia subaracnóidea (HSA), prevenção de acidente vascular cerebral (AVC) em crianças com anemia falciforme e como método complementar no diagnóstico de morte encefálica. O DTC também pode ser usado na investigação do AVC para detecção de shunts direita-esquerda (cardíacos ou extracardíacos), avaliação de microembolia, estenose intracraniana, vasorreatividade, e como método não invasivo para monitoramento de pressão intracraniana (PIC) e autorregulação cerebral.
Objetivos: Objetivamos revisar as evidências mais recentes em relação ao DTC, seus princípios, técnicas e aplicações, principais vantagens e limitações.
Métodos: Efetuamos uma revisão detalhada da literatura acerca do DTC e suas aplicações na avaliação e manejo das doenças cerebrovasculares, além de aplicações no manejo de pacientes neurocríticos.
Resultados: O DTC tem papel forte e bem estabelecido na prevenção de AVC em crianças com anemia falciforme e no manejo de vasoespasmo/isquemia cerebral tardia na HSA. Demais indicações como no AVC e entendimento da hemodinâmica cerebral em pacientes críticos vêm ganhando importância e popularidade.
Conclusões: O DTC é um método útil, seguro e factível para uso em cenários intra e extra hospitalares. É de suma importância para avaliação etiológica nos eventos cerebrovasculares e sua prevenção. Vem ganhando evidência como método não invasivo para estimar pressão intracraniana e autorregulação cerebral, além de ser consagrado como método complementar no diagnóstico de morte encefálica.

Palavras-chave: Doppler transcraniano, ultrassom, hemorragia subaracnoidea, anemia falciforme, acidente vascular cerebral, morte encefálica

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CORRESPONDENCE AUTHOR
Carolina Rouanet, carolrouanet@gmail.com

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INTRODUCTION

Transcranial Doppler (TCD) is a non-invasive, safe, quick to perform and relatively inexpensive neuroimaging method that allows real-time assessment of cerebral blood flow (CBF) velocities in the main basal intracranial vessels [1,2]. Its first description was in 1982 by Aaslid and cols, that noticed that the method was valuable for the detection of vasospasm following subarachnoid hemorrhage (SAH) and for the evaluation of arterial occlusive diseases[3]. Over the next years, the concept that spastic arteries seen on digital subtraction angiography (DSA) have higher velocities on TCD emerges (the sectional area of the vessel is inversely correlated with TCD CBF velocities). Also, higher velocities and their increase may indicate ischemia and impending infarction risk[4].

Since then, TCD has gained increasing importance in the fields of Neurology and neurocritical care, as it enables the evaluation of cerebral hemodynamics with high accuracy, demands no sedation or patient transportation, and is suitable for monitoring critical conditions in a real-time fashion[1,2].

This article summarizes TCD's physical principles, techniques and primary applications in the diagnosis and management of diverse cerebrovascular conditions at the bedside.

METHODS

The literature on the technique procedures of TCD was reviewed using the words *Transcranial Doppler, Cerebrovascular diseases, Stroke, Sickle Cell Disease, Intracranial Hypertension, Brain death*, alone or in combination for search in the databases PubMed, Bireme, Lilacs. Articles from 1982 until nowadays were considered suitable for revision.

RESULTS

The results make up a comprehensive review organized in the sections: 1) Physical principles and TCD technique; 2) Clinical applications: Subarachnoid Hemorrhage and Cerebral Vasospasm, Diagnosis of Right-to-Left Shunt, Microembolic signals, Intracranial artery stenosis and Sickle Cell Disease; 3) TCD study of cerebral autoregulation and vasoreactivity; 4) TCD in intracranial pressure assessment; 5) TCD on the complementary diagnosis of brain death.

1) Physical Principles and technique

TCD is based on the principles of the Doppler effect, which involves the emission of high-frequency sound waves that pass through the skull and reflect off moving blood cells[1,2,5,6]. The blood flow within the vessel is laminar, so the Doppler signal represents a mixture of different Doppler frequency shifts, forming a spectral display of individual red blood cells on the TCD monitor. The parameters measured from this spectral analysis include peak systolic velocity (PSV), end-diastolic velocity (EDV), systolic upstroke or acceleration time, pulsatility index (PI), and mean flow velocity (MFV), all of which are automatically calculated and displayed on TCD screen[2].

Several factors influence CBF measurements in TCD and should be highlighted: age, gender, hematocrit, viscosity, carbon dioxide levels, temperature, blood pressure (BP), and mental or motor activity. CBF velocities in intracranial vessels decrease by an average of 0.3 to 0.5% per year between the ages of 20 and 70. Studies have shown that women usually have higher CBF velocities than men. Hematocrit and viscosity are inversely related to CBF velocities, and measured blood flow velocities (BFV) may increase with higher systemic BP when cerebral autoregulation is compromised[5].

The exam is performed through four cephalic acoustic windows: transtemporal, transorbital, submandibular and suboccipital (Figure 1). The transtemporal window consists of the anterior, middle, and posterior windows, and allows the insonation of intracranial internal carotid artery (ICA) bifurcation, anterior and middle cerebral arteries (ACA and MCA, respectively), and posterior cerebral artery (PCA). The transorbital window is used to evaluate the carotid siphon and the ophthalmic artery, and the suboccipital window, the basilar and vertebral arteries[6].

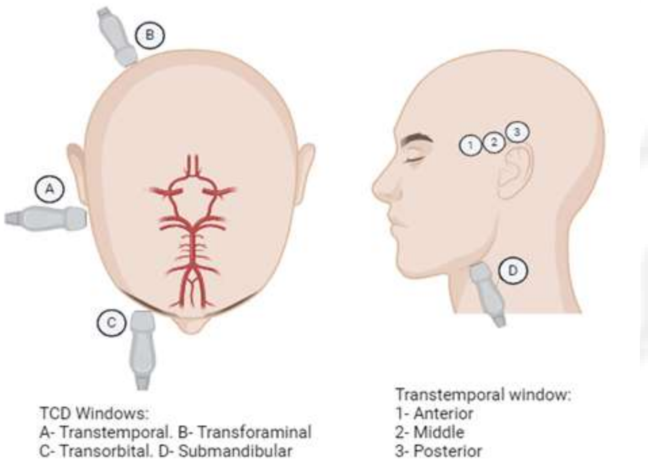

Figure 1. Acoustic windows for Transcranial Doppler (TCD) examination.
TCD – transcranial doppler

Two types of ultrasound equipment are mostly used: B-mode transcranial color-coded duplex (TCCD) and transcranial Doppler (TCD) sonography. TCCD is usually performed using a 2–2.5-MHz probe that combines B-mode imaging (gray-scale ultrasound) with Doppler measurement. B-mode provides a visual image of the blood vessels and surrounding structures, while the Doppler component measures blood flow velocity. Their main advantages are anatomic visualization of the vessels and identification of structural abnormalities (Figure 2).

Figure 2. Transtemporal window insonation with TCCD showing polygon of Willis on Midbrain plane. A) Middle cerebral artery. B) Posterior cerebral artery, P1 segment. C) Posterior cerebral artery, P2 segment. D) Anterior cerebral artery.

TCCD - transcranial colour-coded duplex

TCD identifies the cerebral arteries "blindly", through the spectral analysis and standard criteria: arterial depth, blood flow direction and waveform analysis. Despite not providing a visual image of the vessels, it allows assessment and continuous monitoring of CBF velocity, making this method very useful in multimodal brain monitoring. Advanced parameters such as cerebral autoregulation, critical closing pressure and cerebral compliance can be assessed with TCD, besides the functional tests for evaluating cerebrovascular reactivity[2,7] (Figure 3).

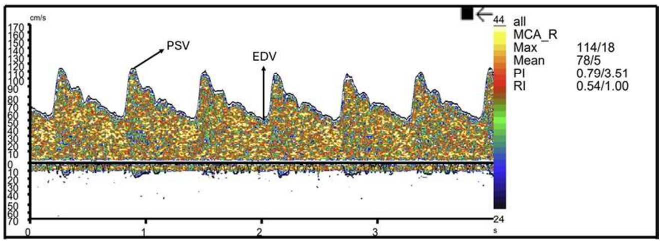

Figure 3. Normal flow on TCD spectral display.

PSV: Peak systolic velocity. EDV: End-diastolic velocity. TCD - transcranial doppler

2) Clinical applications

2.1) Subarachnoid Hemorrhage and Cerebral Vasospasm

TCD plays an important role in the diagnosis and monitoring of vasospasm in patients with aneurysmal subarachnoid hemorrhage (SAH). Cerebral vasospasm, defined as the narrowing of large cerebral arteries observed on vascular imaging, occurs in approximately 70% of SAH patients[9]. Delayed cerebral ischemia (DCI) affects about 30% of patients with SAH, mostly between 4 to 14 days after ictus, and may be associated with cerebral vasospasm[8]. For those who survive the initial bleeding, DCI is one of the main determinants of functional outcome. Therefore, it is recommended to conduct daily or alternate-day monitoring with TCD in patients with SAH, particularly between days 3 and 15 after the onset[6].

Digital subtraction angiography (DSA) is the gold standard for diagnosing cerebral vasospasm; however, it is an invasive procedure, with radiation and iodinated-contrast exposure and limited availability[11]. In contrast, TCD is a widely available and reproducible method that can be performed daily, making it an essential tool in this context. This technique relies on the physical principle (Poiseuille Law) that BFV in an artery is inversely proportional to its cross-sectional area. TCD is more reliable in detecting vasospasm in the MCA than in other cerebral arteries, although there are also criteria for other arteries, albeit with less accuracy (Tables 1 and 2)[11,12].

Table 1. Transcranial Doppler criteria for middle cerebral artery vasospasm

MFV (cm/s)	Lindegaard index	Interpretation
> 120	≤ 3	Hyperemia
≥ 120	3-4	Light spasm + hyperemia
≥ 120	4-5	Moderate spasm + hyperemia
≥ 120	5-6	Moderate spasm
≥ 180	> 6	Moderate to severe spasm
≥ 200	≥ 6	Severe spasm
> 200	4-6	Moderate spasm + hyperemia
> 200	3-4	Hyperemia + light spasm (often residual)
> 200	< 3	Hyperemia

MFV: Mean Flow Velocities

Adapted from Marcos C Lange, Neurossonologia Aplicação Prática, 2018; Manual de Doppler Transcraniano. Academia Brasileira de Neurologia. 2006.

Table 2. Transcranial Doppler criteria for other cerebral arteries (except MCA) vasospasm

Artery	Possible spasm (MFV, cm/s)	Probable spasm (MFV, cm/s)	Definitive spasm (MFV, cm/s)
ICA	> 80	> 110	> 130
ACA	> 90	> 110	> 120
PCA	> 60	> 80	> 90
BA	> 70	> 90	> 100
VA	> 60	> 80	> 90

ACA: Anterior cerebral artery, BA: Basilar artery, ICA: Internal carotid artery, MCA: middle cerebral artery, MFV: Mean flow velocity, PCA: Posterior cerebral artery, VA: Vertebral artery

Adapted from Marcos C Lange, Neurossonologia Aplicação Prática, 2018; Manual de Doppler Transcraniano. Academia Brasileira de Neurologia. 2006.

MFV in MCA greater than 120 cm/s or an increase ≥50 cm/s over a 24-hour period indicate vasospasm, while MVF greater than 200 cm/s suggest severe vasospasm[1,6,11].

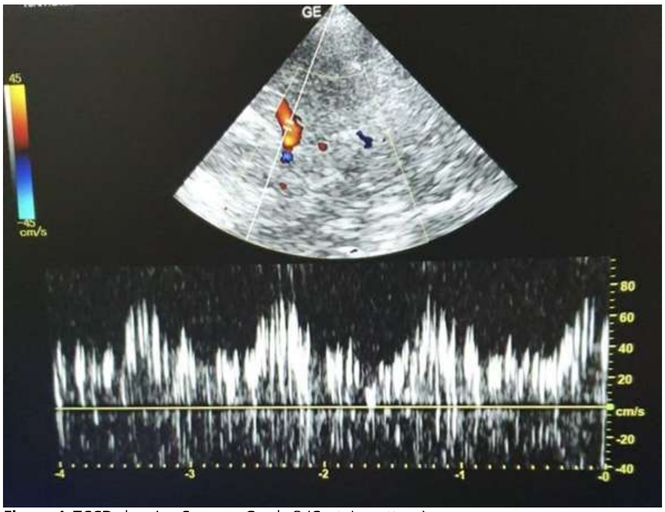

Figure 4. TCCD showing Spencer Grade 3 (Curtain pattern)

TCCD - Transcranial Colour-Coded Duplex

Given that conditions such as anemia and fever can cause a hyperdynamic state and to avoid misinterpretation results, it is recommended to evaluate the Lindegaard ratio (LR), calculated as the MFV of the MCA divided by the MFV of the extracranial ipsilateral internal carotid artery. An LR greater than 3 indicates vasospasm, and an LR greater than 6 suggests severe vasospasm[1,6,11,1].

Several studies have analyzed the correlation between mean MCA flow velocity on TCD and the degree of angiographic vasospasm as assessed by DSA, however with controversial evidence[13,14,16]. Publications have shown high specificity of TCD (94 to 100%) but variable sensitivity (39 to 96%) compared to DSA in the MCA[13]. In a recent systematic review, TCD reached a sensitivity of only 38% compared to DSA[13,15]. Due to this variability in sensitivity, TCD should be used in conjunction with neurological examinations to reflect the patient's clinical condition or alongside another monitoring modality[15].

2.2) Diagnosis of Right-to-Left Shunt

Paradoxical embolism is a known cause of ischemic stroke, characterized by emboli moving from the venous to the arterial circulation through a right-to-left shunt (RLS). Persistent Patent Foramen Ovale (PFO) is the main cause of an RLS shunt; however, up to 11% of RLS cases have extracardiac sources, such as pulmonary arteriovenous fistulas[4].

TCD technique to detect RLS involves the injection of microbubble-contrast agents (typically agitated saline or a saline-air-blood mixture) into a peripheral vein while monitoring the MCA. When bubbles pass through a PFO or other types of RLS, they reach the cerebral circulation and are detected by TCD as high-intensity transient signals (HITS). To increase the sensitivity of the test, the patient performs the Valsalva maneuver (forced exhalation against a closed airway) during the injection to increase the intrathoracic pressure, which temporarily opens the shunt[6]. The degree of shunt on TCD correlates with ischemic stroke risk, so it is essential the quantification of HITS, which can be done through two classifications: the International Consensus and Spencer Criteria (Table 3 and 4) (Figure 5)[17].

Table 3. International Consensus for Right-to-left shunt classification

Grade	Microbubbles (bilateral TCD monitoring)
Grade 0	None
Grade 1	1-10
Grade 2	10-20
Grade 3	> 20, curtain appearance

TCD - transcranial doppler
Adapted from Alexandrov Cerebrovascular Ultrasound in Stroke Prevention and Treatment. Second Edition, 2011.

Table 4. Spencer Logarithmic Scale for Transcranial Doppler grading shunt

Grade	Microbubbles
Grade 0	None
Grade 1	1-10
Grade 2	11-30
Grade 3	31-100
Grade 4	101-300
Grade 5	> 300

Adapted from Alexandrov Cerebrovascular Ultrasound in Stroke Prevention and Treatment. Second Edition, 2011.

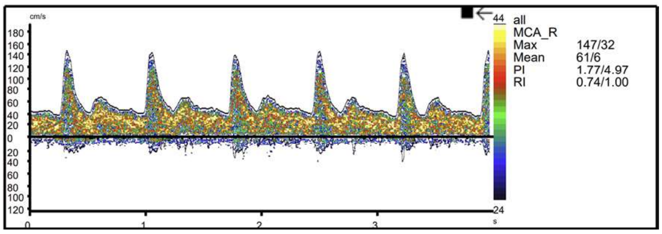

Figure 5. Increased pulsatility of MCA, demonstrating a PI of 1.77.

MCA - middle cerebral artery; PI - pulsatility index

Historically, transesophageal echocardiography (TEE) has been the gold standard method for investigation of cryptogenic stroke, primarily due to the prevalence of PFOs, allowing for direct visualization of intracardiac shunts. Nevertheless, TCD is increasingly being employed in RLS workup due to its ability to detect extracardiac shunts and its lack of sedation requirements, unlike TEE[17,18,20]. In a recent study, a significant shunt, classified as Spencer grade III or higher post-Valsalva maneuver, strongly correlated with high-risk PFOs[18]. Moreover, a recent meta-analysis, which included 29 studies and 2751 patients, showed that the sensitivity and specificity of TCD for PFO diagnosis compared to TEE was 94% and 92%, respectively. In contrast, the sensitivity and specificity of TTE were 82% and 92%[19]. In another study, robotic-assisted TCD detected 63.6% of shunts compared with 20.9% in the standard of care group[20]. Due to its high sensitivity compared to TEE, TCD is a very useful tool, and its accuracy should be tested in further large trials[19].

2.3) Microembolic signals

TCD can detect microembolic signals (MES) which are associated with an increased risk of ischemic stroke, in patients with a previous history of stroke or with cardiovascular risk factors but without previous strokes[22]. TCD detects microembolism as a high-intensity signal (HITS), similar to the signal observed in the investigation of RLS, and the term "spontaneous" means that microembolism is detected without prior contrast injection. The clinical implications of MES are more studied in symptomatic carotid stenosis. Approximately 45% of patients with symptomatic carotid artery stenosis showed MES in the ipsilateral MCA, and the presence of these signals corresponded to a significantly increased risk of subsequent ipsilateral stroke and transient ischemic attacks[6,22,23]. Microembolic signals within the MCA also predict recurrent strokes caused by intracranial MCA-MCA embolization[22,23].

There is also evidence that in patients with carotid stenosis and the presence of MES, antithrombotic therapy should be more intensive. Two randomized controlled trials, CARESS ("Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis") and CLAIR ("Clopidogrel plus aspirin versus aspirin alone for reducing embolization in patients with acute symptomatic cerebral or carotid artery stenosis"), showed that dual antiplatelet therapy reduced significantly the rates of MES compared with medical therapy with aspirin alone in patients with carotid stenosis[24,25].

In asymptomatic carotid disease, TCD can help to identify patients at higher risk of stroke, along with other risk predictors[26]. In the ACES study ("Asymptomatic Embolization for Prediction of Stroke in the Asymptomatic Carotid Emboli Study"), 467 patients with asymptomatic carotid stenosis were monitored for one hour using TCD and followed for two years[27]. The annual risk of stroke or TIA was significantly higher in the group that showed HITS on TCD (7.1% vs. 3%)[27]. This small group of patients could benefit from endarterectomy.

Signs of microembolism have also been studied in cardiac pathologies with high thromboembolic risk, such as atrial fibrillation, mitral stenosis, acute phase of myocardial infarction, dilated cardiomyopathy, metallic and biological prosthesis[6].

2.4) Intracranial artery stenosis

Intracranial stenosis (IS) is defined as a focal or diffuse reduction in the diameter of intracranial arteries, which may or may not be associated with intracranial atherosclerotic disease[6,21]. Around 10% of ischemic stroke patients present with intracranial stenosis, and in Eastern populations, this percentage can reach 30%[6]. TCD has shown high specificity and sensitivity in identifying IS in patients with ischemic stroke. In a recent meta-analysis that included 18 studies, TCCD exhibited a high pooled diagnostic accuracy in stratifying intracranial steno-occlusions when compared to DSA as a reference standard, with a sensitivity of 90% and specificity of 87% [28].

The main parameter considered in the evaluation of IS is the cerebral BFV, since a reduction in vessel diameter leads to an increase in MFV. When the vessel lumen is reduced by 50%, the PSV doubles. However, in cases where there is a reduction of more than 80% in vessel lumen, it is no longer possible to increase velocity, which starts to paradoxically drop. Furthermore, other TCD criteria observed in IS include the following: 1) MFV asymmetry above 30% between concurrently insonated homologous vessels, 2) loss of physiological hierarchy of parameters found in typically insonated segments, 3) turbulent flow, 4) in the pre-stenotic segment, a decrease in the end-diastolic component and an elevation in PI, 5) finally, in the post-stenotic segment, a decline in systolic acceleration and MFV is observed (blunted signal) (Figure 6). In addition to atherosclerotic disease, other conditions associated with IS include vasculitis, inflammatory arteriopathies, dissections, and drug-induced or secondary vasoconstriction[1,2,5,6].

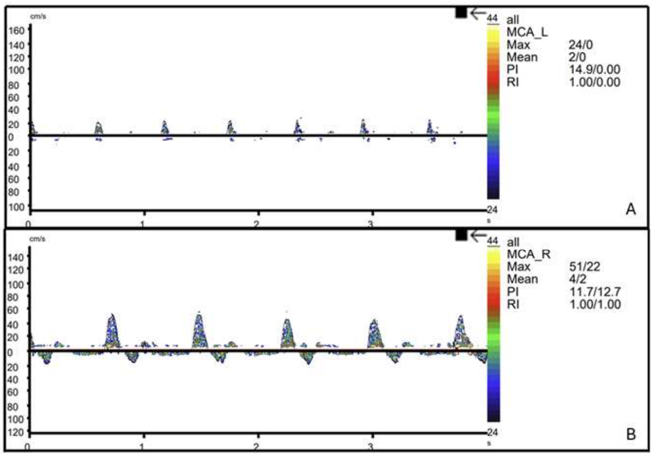

Figure 6. TCD in patients with brain death. (A) short systolic peak in MCA. (B) alternating flow in MCA

MCA - middle cerebral artery; TCD - Transcranial Doppler

2.5) Sickle Cell Disease

Ischemic stroke occurs in 11% of children with sickle cell disease (hemoglobin HbSS), primarily due to stenosis or occlusion of the distal intracranial ICA or proximal MCA. The narrowing of blood vessels leads to increased cerebral BFV. Consequently, TCD contributes to identifying patients with sickle cell anemia who are at a higher risk of developing ischemic stroke[1]. The management of these patients evolved after the publication of the "Stroke Prevention Trial" (STOP) in 1998[29], which evaluated 130 children with a time-averaged mean of the maximum (TAMM) velocities of more than 200 cm/s in MCAs or terminal ICAs with TCD. Children with TAMM higher than 200 cm/s were randomized to receive transfusion or standard care. After a follow-up of 20 months, there was a reduction greater than 90% in relative risk of stroke incidence in the intervention group (one stroke in the 63 children randomized to transfusion versus 11 strokes in the 67 children randomized to standard care).

STOP investigators continued to analyze if children who received blood transfusion, should continue or stop receiving transfusion. So, the STOP-2 trial was performed and showed significantly less reversion to high stroke risk TCD velocities and less ischemic stroke rates in the group that continued to receive transfusion[30]. Thus, those children with sickle cell disease who once qualified for blood transfusions should continue to receive transfusions to sustain the primary stroke prevention benefit. It is important to highlight that not only high BFV indicate risk of stroke, but low TAMM velocities (less than 75 cm/s) in non-transfused HbSS patients are very low and raise concerns about severe proximal stenosis[30].

Based on that evidence, current guidelines[31,32] established recommendations for the TCD frequency in sickle cell disease patients between 2-16 years old according to the TAMM in the MCA (Table 5).

After four years (at least 12 months) of packed red blood cells (pRBC) transfusions, normal TCD and magnetic resonance angiography with no severe vasculopathy, hydroxyurea at maximum tolerated dose can be offered to prevent primary stroke, maintaining pRBC transfusions until the patient reach this dose[31,32]. Other recommendations include the use of the TCD as the device of choice, since the TCCD is not validated in patients with sickle cell disease. Additionally, it is not recommend to perform the exam in a child who is acutely ill, as fever, hypoxia, hypocarbia and worsened anemia may all transiently increase the TAMM, possibly resulting in a TAMM higher than 200 cm/s[31].

3) TCD study of cerebral autoregulation and vasoreactivity

The brain has its intrinsic capacity to maintaining constant CBF despite changes in arterial mean blood

Table 5. Recommendations for the TCD frequency in sickle cell disease patients

TCD result	Max CBF (cm/s)	Exam frequency
Low	< 70	Repeat after 1 month
Normal	< 170	Repeat annually
Low conditional	170-184	Repeat after 3 months - If TCD is normal, repeat annually
High conditional	185-199	Repeat after 1 month: - If high conditional, repeat every 3 months - If two high conditional results, discuss stroke risk and proceed to magnetic resonance angiography or consider starting chronic pRBC transfusions
Abnormal	≥ 200-219	Repeat after 1 month: - If the value remains ≥200 cm/s, discuss the stroke risk and consider chronic pRBC transfusion - If the result decrease to high conditional, repeat in 1 month - If the result decrease to low conditional, repeat in 3 months - If the result is normal, repeat in 1 year.
	≥ 220	Imminent stroke risk, discuss chronic pRBC transfusions

Max CBFV - maximum mean cerebral blood flow velocity; pRBC- packed red blood cell; SCD, sickle cell disease (Hb SS and Hb S/ß0); TCD - transcranial doppler
Adapted from Lobo et al, 2011[26]

pressure (MBP) or cerebral perfusion pressure (CPP) through vasodilation or vasoconstriction of brain resistance vessels (precapillary arteriole). This is called autoregulation[1,2,21]. A sudden change in MBP/CPP leads to an initial immediate change in flow, that, in the normal brain, is restored after a few seconds[1,2,21].

Autoregulation is usually preserved in a range of 50-150mmHg of MBP, leading to prevention of hypo or hyperperfusion[1,2,21] It has a complex pathophysiological mechanism, mainly driven by metabolic, neurogenic and myogenic responses. Cerebral blood vessels are exquisitely sensitive to variations in carbon dioxide partial pressure (pCO2) – and increase in pCO2 leads to vasodilation, while a reduction, to vasoconstriction[1,2,5,21].

Those changes also affect proximal branches of the circle of Willis, thus, are reflected by changes in velocities and waveforms analyzed by TCD, which is called vasomotor reactivity (VMR). MCA velocity changes by 3-4% per mmHg change in end-tidal CO2. A very simple way to access VMR is by analyzing MCA MFV after 30 seconds of breath-holding, which is termed breath-holding index (BHI). It can be calculated by the following equation: BHI = (MFV end – MFV baseline/ MFV baseline) x (100/seconds of breath holding)[5,21]. A normal value is considered above or equal to 0,69[1,2,5]. Silvestrini et al prospectively demonstrated that an impaired BHI is associated with a higher risk of stroke in patients with asymptomatic carotid artery stenosis[34].

Due to autoregulation, vasodilation occurs distally to a proximal stenosis. When it has reached its maximum capacity, no vasomotor response is seen, meaning that any drop in BP may lead to ischemia or hypoperfusion[5,21]. Thus, TCD may be a useful non-invasive method for the evaluation of cerebral autoregulation in the context of arterial stenosis or critical neurological conditions in intensive care units[5,21].

4) TCD in intracranial pressure assessment

The gold standard intracranial pressure (ICP) monitoring methods involve invasive procedures, with high risk of complications, therefore, efforts have been made to develop non-invasive ICP monitoring methods. Examples of non-invasive methods include physical examination, brain imaging, optic nerve sheath ultrasound, fundoscopy, metabolic changes measurements (near-infrared spectroscopy [NIRS]), neurophysiological studies and TCD[34]. From a pathophysiological point of view, increased ICP affects CBF velocities resulting in low EDV, peaked waveform and a higher PI in TCD monitoring[5]. Some studies have shown a good correlation between ICP and PI values in patients with traumatic brain injury. However, the results are controversial, and recommendations cannot be made regarding the application of solely the TCD in the assessment of ICP[5].

5) TCD on the complementary diagnosis of brain death

TCD is one of the complementary methods used in the diagnosis of brain death. It has 100% specificity and 88% sensitivity in identifying cerebral circulatory arrest, when compared to DSA, which is the gold standard[6]. As previously mentioned, as ICP rises, end-diastolic flow velocity decreases and the curve becomes peaked. When intracranial pressure equals diastolic pressure, EDV disappears, and even greater increases in intracranial pressure result in inversion of EDV, called alternating flow (anterograde flow in systole and retrograde flow in diastole), and ultimately can be observed only short systolic peaks. The last two patterns are indicative of cerebral circulatory arrest, compatible with the diagnosis of brain death[5,6,21].

For the performance of TCD, Brazilian guidelines[35] recommend the patient to be at the supine position, with systolic BP above 90 mmHg, heart rate above 60 bpm, and no hypoxemia (SpO2 > 95%). The technical protocol includes bilateral evaluation of the MCAs through the transtemporal window, of the VAs bilaterally through the transforaminal window, and the BA. Absence of flow must be observed in all mentioned arteries to establish the diagnosis of brain circulatory arrest. To the absence of flow can be interpreted as indicative of cerebral circulatory arrest, the patient must have undergone a TCD during the same hospital stay with confirmation of adequate CBF. In the absence of a transtemporal window, the evaluation of the MCAs can be substituted by examination of the carotid siphon bilaterally through the transorbital window[35].

CONCLUSION

TCD is a non-invasive, low-cost, safe and readily available exam, which has been increasingly used at the bedside for both diagnosis and monitoring of multiple neurological injuries. Recent studies have demonstrated the benefits of TCD in several medical applications, including guiding transfusion decisions in patients with sickle cell anemia, monitoring patients with subarachnoid hemorrhage (SAH), and detecting perioperative microembolism. Its usage has also been expanding in the etiological investigation of ischemic stroke, among other conditions. Promising applications currently under investigation include evaluation of arteriovenous malformation, assessment of recanalization following thrombolysis for acute ischemic stroke, sonothrombolysis, intraoperative monitoring, neuroprognostication of post cardiac arrest and evaluation of CBF after cerebrovascular bypass. With the advancement of technology, it is likely that we will see new future indications for TCD.

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