JOURNAL OF Cardiovascular Echography

J Cardiovasc Echogr. 2016 Apr-Jun; 26(2): 28–41. PMCID: PMC5224659
doi: 10.4103/2211-4122.183746: 10.4103/2211-4122.183746 PMID: 28465958

Transcranial Doppler Ultrasound: Physical Principles and Principal Applications in Neurocritical Care Unit

Antonello D'Andrea, Marianna Conte, Raffaella Scarafile, Lucia Riegler, Rosangela Cocchia, Enrica Pezzullo, Massimo Cavallaro, Andreina Carbone, Francesco Natale, Maria Giovanna Russo, Giovanni Gregorio,[1] and Raffaele Calabrò

Department of Cardiology, Integrated Diagnostic Cardiology, Second University of Neaples, Monaldi Hospital, Neaples, Italy

[1]*Department of Cardiology, San Luca Hospital, Vallo della Lucania, Salerno, Italy*

Address for correspondence Dr. Antonello D'Andrea, Via M. Schipa 44, 80122, Naples, Italy. E-mail: antonellodandrea@libero.it

Abstract

Transcranial Doppler (TCD) ultrasonography is a noninvasive ultrasound study, which has been extensively applied on both outpatient and inpatient settings. It involves the use of a low-frequency (≤2 MHz) transducer, placed on the scalp, to insonate the basal cerebral arteries through relatively thin bone windows and to measure the cerebral blood flow velocity and its alteration in many different conditions. In neurointensive care setting, TCD is useful for both adults and children for day-to-day bedside assessment of critical conditions including vasospasm in subarachnoid hemorrhage, traumatic brain injury, acute ischemic stroke, and brain stem death. It also allows to investigate the cerebrovascular autoregulation in setting of carotid disease and syncope. In this review, we will describe physical principles underlying TCD, flow indices most frequently used in clinical practice and critical care applications in Neurocritical Unit care.

Key Words: Brain stem death, cryptogenic stroke, mean cerebral brain flow, Neurocritical Unit Care, paradoxical embolism, patent foramen ovale, subarachnoid hemorrhage, transcranial Doppler ultrasonography, traumatic brain injury, vasospasm

INTRODUCTION

Transcranial Doppler (TCD) ultrasonography is a noninvasive ultrasound (US) study, which was introduced in clinical practice in 1982,[1] since then it has been extensively applied on both out-patient and inpatient settings.

TCD ultrasonography involves the use of a low-frequency (≤2 MHz) transducer, placed on the scalp, to insonate the basal cerebral arteries through relatively thin bone windows and to measure the cerebral blood flow velocity (CBFV) and its alteration in different cerebrovascular diseases (CVDs) and traumatic brain injuries.

It is inexpensive, repeatable, and allows continuous bedside monitoring of CBFV, which is particularly useful in the intensive care setting.[2]

TCD examinations have gained an important role in the very early phase of critical cerebral pathologies, as well as during follow-up of patients with chronic CVDs.

It is also useful on both adults and children to diagnose and monitor vasospasm (VSP) after subarachnoid hemorrhage (SAH)[3] of different etiologies (aneurysm rupture and traumatic brain injury [TBI]),[4,5] and cerebral hemodynamic changes after stroke including cryptogenic stroke.

It allows to investigate cerebral pressure autoregulation and for the clinical evaluation of cerebral autoregulatory reserve.[6]

TCD has important clinical application in the management of patients with sickle-cell disease, brain stem death,[7] and raised intracranial pressure (ICP).[8] Moreover TCD allows for intraoperative monitoring,[9] evaluation of vasomotor function,[10] and assessment of cerebral microembolism due to right to left cardiac shunts.[11]

Other clinical applications of TCD include monitoring of cerebral circulation and embolization during cardiopulmonary bypass, carotid endarterectomies, and carotid artery stenting.

In this review, we will describe physical principles underlying TCD, flow indices most frequently used in clinical practice, and critical care indications for this imaging modality.

ANATOMY OF MAIN INTRACRANIAL ARTERIES

For better understanding of TCD findings and its applications in clinical setting, can be useful to make a brief description about the anatomy of intracranial arteries of major clinical interest: Internal carotid artery (ICA), middle cerebral artery (MCA), anterior cerebral artery (ACA), and posterior cerebral artery (PCA).

The ICA is the terminal branch of the common carotid artery, together with the external carotid artery.

It starts at C3 and C5 vertebral level, and it is divided into seven segments (named from C1 to C7).

The ICA gives rise to two terminal branches: MCA and ACA, the MCA is the most frequently insonated artery during TCD examinations.

It originates from the ICA, and it runs into the lateral sulcus where it then branches and gives blood to many parts of the lateral cerebral cortex. It can be subdivided into four parts:

- The horizontal segment also called the sphenoidal segment M1
- The insular segment also called M2 segment
- The opercular segments also called M3 segment
- The cortical segments also called the M4 terminal segments.

The ACA is smaller than MCA, and at the level of corpus callosum, is divided into pericallosal and callosomarginal branches.

The PCA represents the terminal branches of the basilar artery (BA) and irrigates the occipital lobes and posteromedial temporal lobes.

PROBE AND SCANNING PROCEDURES

In clinical practice, the most frequently used transducer is a Pulsed Doppler sectorial probe with a 2.0–3.5 MHz emission frequency.

The probe can then be fixed to the scalp with a headband so that the same angle of insonation for continuous flow velocity recordings is maintained throughout the examination.

TCD is conducted using either transcranial color-coded duplex sonography, in which it is displayed a two-dimensional color-coded image[12] or once the desired blood vessel is insonated, blood flow velocities may be measured using Pulsed wave (PW) Doppler.

The TCD with combined ColorFlow and power Doppler allows direct imaging of the intracranial arteries, their anatomic course, diameter, and relationships with the adjacent structures.

To get a better quality of the Doppler signal in spite of background noises, the TCD devices are equipped with a larger sample volume compared to other PW Doppler probe.

In standard TCD examination should be recorded bilateral PW Doppler tracing lasting at least 10 cardiac cycles after a 30 s stabilized recording period.

ACOUSTIC WINDOWS AND SCANNING PLANE

The transmission of an US beam through skull is influenced by structural characteristics of the diploe bone: The almost complete absence of bone spicules makes the penetration of the US similar to conventional “acoustic windows” consenting the visualization of intracranial vessels.

First of all, the patient should be lying in supine position, with his head and shoulders on a pillow.

In general terms, transcranial US study can be performed using two main scanning planes: The axial and coronal planes at a depth that allows to display also the contralateral vessels.

The axial scan is the one most commonly used, and it allows two different types of imaging planes: The mesencephalic and diencephalic views.

In clinical practice, the most relevant scanning plane for the study of cerebral arterial vessels is the mesencephalic plane, so our review will focus mainly on this view.

It is obtained by positioning the probe parallel to the zygomatic arch. At this level can be identified the hypoechogenic “butterfly-shaped midbrain,” located usually in the middle of the screen.

In the 75% of cases, can be also detected the posterior communicating arteries if they have enough relevant diameter.

Regarding Doppler study of intracranial arteries, in clinical practice, there are four acoustic windows that can be used for TDCS.

The temporal window is situated above the zygomatic arch, anterior to the tragus, using an axial plane to obtain a mesencephalic view, with the patient's head in the anteroposterior position [Figure 1].

This window can be divided into anterior, middle, and posterior zone and allows to identify the MCA in its M1 and M2 segments.

From this approach can be also visualized A1 segment of the ACA, P1 and P2 segments of the PCA and C1 segment of the carotid siphon [Figure 2].

In this temporal view can be also seen the communicating arteries - anterior and posterior - and the distal end of the BA.

Approximately, 10–20% of patients have inadequate transtemporal acoustic windows depending on patient age, female sex, and other factors affecting the temporal bone thickness.[2,13,14]

In the occipital window, the probe must be positioned on the median suboccipital line, and the patient should be sitting or lying down with the head turned to opposite direction respect to the operator with the chin lowered toward the shoulder. With US beam passing through the foramen magnum in this window, it can be visualized the intracranial segment of the two vertebral arter-

ies (VA) and the basilar trunk.

In the orbital window, the transducer is put perpendicularly to the eyelid, with patient's eye closed and looking on the opposite side respect to the probe. This approach allows to insonate the ophthalmic artery and the C2, C3, and C4 segments of the carotid siphon through the foramen of the ocular cavity. The limitation of this approach is represented by the potential retinal injuries caused by the US beam: it is advisable to reduce power of the device 10–15% respect to transtemporal scan.

In addition to the above-mentioned views, it can be also used the submandibular window.

This approach is employed in the case of impossibility to standard windows.

Middle cerebral artery

It is the most frequently insonated intracranial vessel in clinical practice because it is easily delineated through the temporal window. It collects nearly 60–70% of the ICA blood flow, so its evaluation can be taken to represent almost total blood flow to one hemisphere.

In practice, MCA is detected at a depth of 45–60 mm, and the blood flow is directed toward the probe.[15]

The identification of the sphenoid bone, through the “butterfly wing sign,” guides MCA visualization in almost all patients, with a constant depth of 59 ± 3 mm.[16]

The time to achieve an adequate echographic image of MCA is about 50 ± 20 s.[16]

PHYSICAL PRINCIPLES AND TRANSCRANIAL DOPPLER INDICES

In physical terms, the ultrasonic beam emanated by the probe crosses the skull and is reflected back from the erythrocytes flowing in blood vessels, with a change in its frequency (the Doppler shift f) that is directly proportional to the velocity (V) of the erythrocytes.

In the intracranial vessels, like in other vital organs (liver, kidney, and heart), the Doppler signal shows a prominent diastolic component.

The following equation derived from Doppler principles described above is used for the estimation of CBFV with TCD:

$$V = \frac{(c \times f)}{2 \times f_0 \times \text{costheta}}$$

where c is the speed of the incident US wave, f_0 is the incident wave pulse frequency, theta is the angle of the reflector wave relative to the US emission beam.[17]

Mean CBFV is derived through the spectral envelope of Doppler signal as indicated by following formula:

Mean CBFV = (PSV + [EDV × 2])/3

where PSV is peak systolic velocity, and end diastolic velocity (EDV) is end-diastolic blood flow velocity[3,18,19] [Figure 3].

By the Bernoulli principle, the correlation between velocity and pressure exerted by blood flowing is characterized by a decrease of pressure exerted by the fluid as the velocity of flow increases.

Moreover, it should be remembered that by the continuity principle, the CBFV in a given artery is inversely related to the cross-sectional area of the same artery.[19,20]

Hence, TCD ultrasonography gives an indirect evaluation of the diameter of intracranial vessel through the analysis of blood flow velocity.[19]

There are many physiologic factors affecting CBFV: Age, hematocrit, gender, fever, metabolic factors, pregnancy, menstruation, exercise, and brain activity[21,22,23,24] [Table 1a and b].

In fact, when mean CBFV is increased, it suggests stenosis, VSP, or hyperdynamic flow.

On the other hand, a decreased value indicates hypotension, raised ICP, or brain stem death.[21]

A segmental arterial stenosis or VSP is characterized by an increased mean CBFV within a 5–10 mm tract by >30 cm/s compared with the healthy contralateral arterial tract.[25]

Despite the widespread diffusion of two-dimensional echo-Doppler, some uncertainties remain in clinical practice about the direct vessel area measurements. TCD may fail to recognize cerebral VSP in the case of contemporary mean CBFV and intracranial vessel diameter decrease.[26,27]

Other clinically significant parameters measured with TCD examination are represented by Gosling's pulsatility index (PI) and/or Pourcelot resistivity index (RI) and the Lindegaard ratio (LR) [Figure 3].

The first two give an estimation of downstream resistance in cerebral circulation.

Gosling's PI is calculated as:

PI = (PSV − EDV)/mean CBFV[28]

The Gosling's PI reference range is between 0.5 and 1.19.[28]

In presence of proximal stenosis or occlusion, the PI may be lower than 0.5 because of downstream arteriolar vasodilation; instead, a distal occlusion or constriction shall increase the PI above 1.19 due to increased downstream resistance.[29]

PI is directly related with ICP: A PI variation of 2.4% is reflected by a 1 mm Hg shift of ICP in the same direction.[30]

When the ICP is raised above 20 mm Hg, the PI has been proposed as an alternative estimation of ICP instead of direct measurement.[31,32,33]

Moreover, it has been also demonstrated a significant correlation between the cerebral perfusion pressure (CPP) and PI.[12,33]

The Pourcelot RI is calculated as:

RI = (PSV − EDV)/PSV

A Pourcelot RI value above 0.8 indicates increased downstream resistance.

RI alteration reflects similar disease patterns as those described above with an abnormal PI.[33] It has been observed that RI represents also a good estimation of elevated ICP in different intracranial pathologies. However, when compared with the PI, the RI index is less sensitive to ICP variations[32] [Table 2].

The LR permits to differentiate between hyperdynamic flow and VSP. It is calculated as:

LR = MCA mean CBFV/extracranial ICA mean CBFV[34]

This ratio tends to increase in relation to the severity of VSP.

Normal reference range is from 1.1 to 2.3 and in the absence of VSP is lower than 3.[34]

When the CBFV is elevated but the LR ratio is lower than 3, the elevation is considered to be

caused by hyperemia because patients after of acute SAH (aSAH) are often treated following so-called triple-H therapy: Hypertension, hypervolemia, and hemodilution.

In case of a ratio more than 6, there is a severe VSP.[20,35,36]

Hence, in summary, LR defines the severity of VSP:

MCA mean CBFV/extracranial ICA mean CBFV >3 mild to moderate VSP

MCA mean CBFV/extracranial ICA mean CBFV >6 severe VSP.

Moreover, for detecting the severity of BA VSP, it is calculated the modified LR:

BA mean CBFV/left or right extracranial VA mean CBFV

LR modified: 2–2.49 possible VSP

LR modified: 2.5–2.99 moderate VSP

LR modified: >3 severe VSP [Table 3].

There are few studies which have investigated the mean CBFV variation with TCD in side-to-side as well as in day-to-day.[21,37,38]

The evidence brought by these works suggests that side-to-side variation of more than 14% should be considered abnormal, and most individuals (95%) should have day-to-day variation of mean CBFV <10 cm/s.[21,38]

VASOSPASM AFTER SUBARACHNOID HEMORRHAGE: DIAGNOSIS AND MONITORING ON TRANSCRANIAL DOPPLER

Symptomatic VSP is a frequent complication of aSAH. It should be considered that 25% of patients affected by aSAH develop clinical delayed ischemic deficits due to VSP.[4,13,39,40,41]

The delayed VSP of the cerebral intracranial arteries is angiographically detected in up to 70% of patients affected by SAH and usually develops between 4 and 17 days after acute episode.[20,42] Sometimes, in 13% of cases, it has been described within 48 h.[43,44,45,46,47,48] When it' is still found up to day 20 by TCD,[49] morbidity and mortality are considered to increase significantly up to 20%.[12,48,50,51]

VSP is characterized by a decrease in blood flow through cerebral regions after aSAH secondary to reflex vasoconstriction of intracranial arteries.[20]

The exact mechanism causative of delayed cerebral ischemia (DCI) is not clearly understood.

Clinically, the terms “delayed ischemic neurologic deficit and DCI” have been introduced to describe symptomatic VSP.

Angiography is considered the gold standard to detect VSP but it is an invasive technique and not useful for dynamic monitoring.[2,52] Angiographic VSP, identified by digital subtraction angiography and computed tomography angiography (CTA), has been diagnosed up to 50–70% of patients affected by aSAH and about half of them showed clinical symptoms.[53]

TCD ultrasonography is a noninvasive, repeatable, and relatively inexpensive imaging test and it could be used in patients affected by aSAH for diagnosis and monitoring of VSP.[54] It can identify cerebral hemodynamic changes, diagnosing VSP before appearance of clinical neurologic deficits, and can suggest earlier intervention.[55]

Hence, in Neurocritical Care Unit (NCCU), daily TCD monitoring is warranted for the management of patient affected by aSAH: The timing of the development and resolution of VSP can guide therapeutic strategies. TCD also can monitor the efficacy of interventional procedures such as transluminal balloon angioplasty[9,56] and can identify patients at higher risk of developing DCI.

TCD is able to diagnose MCA and BA VSP with a good sensitivity and specificity. A systematic review of 26 studies confronting TCD with angiography has shown that MCA mean CBFV >120 cm/s detected by TCD carries 99% specificity and 67% sensitivity to identify angiographic VSP of ≥25%.[57] In a retrospective study of 101 patients, MCA mean CBFV >120 cm/s, had 72% specificity and 88% sensitivity to detect angiographic VSP ≥33%, mean flow velocity (MFV) <120 cm/s had a negative predictive value (NPV) of 94%.[58] Moreover, mean CBFV >200 cm/s carried 98% specificity and 27% sensitivity and a positive predictive value (PPV) of 87% for detection of angiographic VSP of ≥33%.[58] Therefore, mean CBFV <120 cm/s and >200 cm/s could predict both absent and present MCA VSP, respectively.

TCD derived LR permits also to differentiate hyperdynamic flow from VSP.

For MCA VSP, it is calculated as MCA mean CBFV/extracranial ICA mean CBFV [Table 3]:

MCA mean CBFV/extracranial ICA mean CBFV > 3 indicates mild to moderate VSP.

MCA mean CBFV/extracranial ICA mean CBFV > 6 indicates severe VSP.

However, its usefulness is limited as it does not increase the identification of MCA VSP or development of DCI.[59]

Thus, TCD, compared with angiography as the gold standard, showed high specificity and high PPV for MCA VSP detection, making it a very useful diagnostic tool in this setting.[57]

TCD criteria for BA VSP have not been universally defined yet [Table 3].

Sviri *et al*.[53] argued that the CBFV ratio (LR BA/VA) between the BA and the extracranial VA is related to the degree BA narrowing (0.648; $P < 0.0001$).

A BA/VA ratio (LR BA/VA) over 2.5 with BA velocity higher than 85 cm/s was 86% sensitive and 97% specific for BA narrowing of more than 25%.

A BA/VA ratio over 3.0 with BA velocities higher than 85 cm/s was 92% sensitive and 97% specific for BA narrowing of more than 50%.

The investigators so concluded that the BA/VA ratio increases the sensitivity and specificity of BA VSP diagnosis by TCD.

Specificity could be brought up to 100% with MFV >95 cm/s.[60]

Moreover, the modified LR BA/VA >3 has a strong correlation with BA diameter, in 100% of patients with VSP >50%.[61]

Therefore, the reported evidences indicate that TCD is highly predictive of angiographically demonstrated VSP in the MCA, but its diagnostic accuracy is lower to identify VSP in the BA.[62,63]

For VSP detection after aSAH in ACA and PCA territory, TCDs diagnostic performance has revealed quite insufficient. In a study involving 57 patients undergone TCD examination within 24 h of angiography, an ACA MFV ≥120 cm/s showed an 18% sensitivity and 65% specificity to detect VSP and a PCA MFV ≥90 cm/s had 48% sensitivity and 69% specificity to detect VSP.[64]

Therefore, caution should be used to make therapeutic decisions based only on the absence of VSP of ACA or PCA by TCD.

Hence, an increased mean CBFV on TCD is highly predictive of VSP of main intracranial arteries after aSAH. It is of critical importance to evaluate day-to-day changes in CBFV: Mean CBFV raising of 50 cm/s or more within 24 h[65] or mean CBFV increases of >65 cm/s per day from day 3 to 7[13] indicates high risk for DCI, which is related to adverse outcome.

In conclusion, the association of clinical examination and different imaging techniques such as CTA and TCD should be used for diagnosis of VSP after aSAH instead of the single independent tests.[66]

The American Heart Association states that TCD could be considered a valid diagnostic tool to identify and to monitor the development of VSP on the management of aSAH.[67]

TRANSCRANIAL DOPPLER STUDY OF CEREBRAL AUTOREGULATION: ITS APPLICATION IN ACUTE SUBARACHNOID HEMORRHAGE, CAROTID DISEASE, AND

SYNCOPE

Cerebral autoregulatory mechanism is a homeostatic function of local brain circulation which keeps CBF constant throughout a wide range of CPP (estimated between 50 and 150 mm Hg).[36]

Dysfunction of cerebrovascular autoregulation has been shown in TBI,[68] stroke,[69] carotid disease,[70] and in syncope although there is still uncertainty about its pathophysiological role in this setting.[71] Evaluation of cerebrovascular autoregulation can give useful prognostic information in these conditions.[72]

The first evidence regarding physiologic cerebral circulatory autoregulation came from works adopting a static approach measuring CBF after a pharmacologic stimulus.[72]

Following the introduction of TCD, CBFV could be used as an estimate of CBF, allowing dynamic monitoring of local CBF.

This approach minimized the influence of potential confounding factors such as oscillation in PaCO2 and autonomic neural activity, which can affect CBF in steady state conditions some hours after pharmacologic stimulus application.[72,73]

TCD performed simultaneously with thigh cuff deflation was used for the first times by Aaslid in 1989,[74] after this, many different nonpharmacologic stimuli were adopted to provoke a pressure modification, such as carotid artery compression,[75] Valsalva maneuver,[76] head-up tilting,[77] and negative pressure applied to lower portion of the body.[71,78]

Although TCD is able to study dynamic cerebral autoregulatory responses, often in clinical practice are used static methods to evaluate autoregulatory function.[71]

In particular, the static autoregulatory index (sARI), which is the ratio between the percent of change in cerebrovascular resistance (CVR) and the percent of change in CPP.

$$\text{sARI}^{[79]} = \frac{\%\,\text{change in CVR}}{\%\,\text{change in CPP}}$$

This index is used to classify autoregulatory function from 0 (no response) to 1 (full response).

Anyway, it should be kept in mind that static methods need pharmacologic or mechanical stimulations which may not be allowed in critically ill patients.[69,72,80]

Regarding dynamic study of cerebral autoregulatory function, no index can be considered as gold standard.[81]

The Mx index expresses the correlation between CPP and m CBFV: A positive correlation means that blood flow is pressure-dependent and absent autoregulation, a negative correlation is found when autoregulatory function is preserved.[80,82] A pitfall of this index is that there could be a significant correlation but with negligible slope.[72]

Tiecks *et al*.[79] introduced the dynamic autoregulatory index (dARI), it is based on fitting the measured CBFV response curve, after a pressure change, to one of 10 theoretical CBFV response graphic representations, ranging from curve 0 (no autoregulatory function) to curve 9 (fully unaffected autoregulation).[79]

In subjects affected by ICA stenosis, derangement of autoregulatory function can represent a marker of high risk of stroke, and so it can be used to guide treatment toward revascularization.[70,83]

In fact, a significant decrease in dARI and increase in Mx indexes have been reported in patients with ipsilateral steno-occlusive of ICA, with a significant correlation with the severity of stenosis.[70,84] However, significantly abnormal dARI and Mx indexes were only found in subjects with severe (>80–90%) stenosis and no relevant difference in Mx was shown between symptomatic and asymptomatic subjects.[70,84]

In the setting of severe SAH, Lang *et al*.[83] studied cerebral autoregulation through continuous monitoring of blood pressure and CBF-velocity recording in 12 patients, confronted with 40 controls. Autoregulatory function was impaired when compared with control subjects ($P < 0.01$ for days 1–6 and $P < 0.001$ for days 7–13). They suggested that TCD could evaluate the entity of autoregulatory dysfunction in patients SAH and a derangement of autoregulation foretells VSP. Moreover, the presence of VSP was associated with worsening of autoregulatory response and the degree of cerebral autoregulatory dysfunction in the 1st days after the event (days 1–6) has a negative prognostic value.

In stroke patients, TCD showed a consistent ipsilateral cerebral autoregulation dysfunction, which was associated with the need of surgical decompression, the severity of neurological damage, and poor outcome.[84]

Regarding its role in syncope, there is still uncertainty about a possible contribution of cerebral autoregulatory dysfunction in this condition.[71]

Many methodological issues of TCD limit the application of this technique in clinical practice for the evaluation of cerebrovascular autoregulation.

The presence of many different static and dynamic stimuli used in many different studies of this subject, without a reference gold standard methodology to confront with and the absence of a single reference value to define an impaired autoregulatory function impede the comparison and

synthesis of different study results.[69,71,85] Moreover, many published works have been conducted with small samples and are statistically underpowered.[71]

In conclusion, the TCD study of cerebral autoregulation is complicated by its technical shortcomings.

TCD studies adopt CBFV as a noninvasive estimate of CBF, but CBFV is directly correlated to CBF assuming that cross-sectional area of cerebral arteries is constant.[86] In addition, since the majority of TCD studies is focused on MCA, alterations of autoregulatory function of posterior cerebral vasculature or in regional cortical vessels may be overlooked.[69]

In conclusion, TCD imaging represents a promising technique for the study of cerebral autoregulatory function, thanks to its good temporal resolution, noninvasive approach, and good cost-benefit ratio. Autoregulation dysfunction has been documented and has a prognostic role in the setting of aSAH and stroke.

The involvement of cerebral autoregulation in syncope is still unclear.

TRANSCRANIAL DOPPLER IN ACUTE ISCHEMIC STROKE: DIAGNOSIS AND PROGNOSIS

The American Academy of Neurology (AAN) Report of the Therapeutics and Technology Assessment Subcommittee states that TCD can accurately identify acute MCA occlusions with a sensitivity, specificity, PPV, and NPV higher than 90%,[87] whereas for occlusion of ICA siphon, VA, and BA shows 70–90% sensitivity and PPV and very high specificity and NPV.[87]

In the setting of acute stroke, TCD has been confronted with magnetic resonance angiography (MRA) and CTA:[88,89,90] It has been especially used to assess steno-occlusive pathology of intracranial vessels such as the terminal ICA, ICA siphon, and MCA.

TCD is 100% specific and 93% sensitive for identification of MCA lesions, whereas MRA had a sensitivity of 46% and a specificity of 74% in the assessment of intracranial arteries.

In the emergency department in patients with suspected acute cerebral ischemia, bedside TCD can give real-time information about CBF adjunctive to that obtained by CTA.[90]

In ischemic stroke, TCD evidence of complete intracranial arterial occlusions predicted worse neurologic outcome, disability, or death after 90 days in 2 studies.[91,92] Normal TCD findings instead predicted early neurological improvement.[87,93]

In patients with acute ICA thrombosis, TCD evidence of arterial occlusion together with stroke severity at 24 h and CT lesion size had proven independent predictive factors of outcome to 30 days.[91]

Performing a TCD examination in the first 24 h of stroke symptom onset greatly increases the ac-

curacy of early stroke subtype diagnosis (hemorrhagic versus ischemic). Moreover, early and accurate detection of arterial occlusion guides emergency management in patients with acute ischemic cerebrovascular accident.

It is universally recognized that clinical course of stroke may present either spontaneous improvements or worsening in relation to dynamic changes in CBF. Thus, the detection of such hemodynamic changes with the use of TCD may have an important prognostic role.

CBF before and after the administration of thrombolytic agents in ischemic stroke is described by the thrombolysis in brain ischemia (TIBI) grading system:[93] Residual flow is classified as either 0: Absent, 1: Minimal, 2: Blunted, 3: Dampened, 4: Stenotic, or 5: Normal.[94]

TIBI grade and its improvement postthrombolysis are related to severity, mortality, and clinical recovery in ischemic stroke.[94,95,96,97]

A meta-analysis has shown that recanalization detected by TCD within 6 h of symptom onset is related to clinical outcome at 48 h (odds ratio [OR]: 4.31, 95% confidence interval [CI]: 2.67–6.97) and functional status at 3 months (OR: 6.75, 95% CI: 3.47–13.12).[98] Moreover, an abrupt increase in TIBI flow or gradual increase over 30 min denotes more effective recanalization and is related to the better short-term outcome on the National Institute of Health Stroke Scale score, compared with flow restoration having a place after more than 30 min.[96]

Mortality is higher in MCA occlusion versus patent MCA on admission in patients without thrombolytic treatment (OR: 2.46 95% CI: 1.33–4.52) and also when MCA occlusion persists hours after tissue plasminogen activator (tPA) bolus.[97,98] Furthermore, applying TIBI score to TCD early reocclusion (flow decrease ≥1 TIBI grade, within 2 h) after thrombolysis (tPA) can be recognized, which may present in up to 34% patients with initial reperfusion.[97] Early reocclusion predicts a significantly worse outcome at 3 months and a higher in-hospital mortality compared to sustained recanalization.[97]

Hence, daily TCD examinations can be useful to recognize dynamic changes in cerebral circulation more time-effectively than a single neuroradiological study. Seriated evaluation of cerebral hemodynamics in patients with acute cerebral ischemia improves the diagnostic accuracy and gives valuable information about monitoring and decision making.

In conclusion, TCD represents a low-cost and readily repeatable diagnostic imaging test characterized by sensitivity and specificity >80% for ICA and MCA occlusion.[82,84]

It also gives useful information about prognosis in MCA occlusion.[82,88,89] However, CTA and MRA should still be used as first-line imaging tests in ischemic stroke because TCD is operator dependent and has low diagnostic accuracy for posterior circulation occlusive pathology.[99]

SICKLE-CELL DISEASE AND ISCHEMIC STROKE

Patients with sickle cell disease are considered at high risk for brain injuries such as subclinical infarction, acute stroke, and hemorrhage. The prevalence of ischemic stroke in this setting is 600 for 100,000 patient years.[100]

The intracranial arteries more frequently involved are ICA, proximal MCA, and ACA. Stenosis or occlusion of these vessels is a result of adhesion of sickle cells to the vascular endothelium.

In asymptomatic children, CBFV >200 cm/s is related to an increased risk of stroke of 10,000 per 100,000 patient years[101] and the treatment with blood transfusion can lower the risk of stroke by >90%.[102] So for children between 2- and 6-year-old affected by sickle-cell anemia, it is recommended to perform a screening by TCD on semestral or annual basis.

On TCD, screening mean maximum CBFV in bilateral MCA, bifurcation, distal ICA, ACA, PCA, and BA is measured.[103] Patients with a time averaged mean maximum CBFV in all arteries of <170 cm/s are considered normal.[103] If a CBF - >200 cm/s in any of above-mentioned vessels is detected, blood transfusion is indicated to lower pathologic sickle hemoglobin to <30% of total hemoglobin to decrease the risk of stroke.[103]

TRAUMATIC BRAIN INJURY AND BRAIN STEM DEATH

TBI represents, among neurological conditions, the principal cause of morbidity and mortality in people under 45 years of age.[104] It is characterized by triphasic pattern in CBF: Hypoperfusion at time 0, hyperperfusion between 24 and 72 h, VSP from days 4 to days 15, and finally by raised ICP.[104,105]

Final outcome of patients depends on two main causes:

1. The initial traumatic injury, which takes place at time of accident and
2. The secondary consecutive pathogenic responses which represent consecutive pathologic processes starting at the moment of trauma and leads to late clinical manifestations (e.g., DCI due to VSP and intracranial hypertension are the most important secondary injuring factors).

TCD allows noninvasive and repeatable bedside assessment of posttraumatic cerebrovascular hemodynamic alterations, providing useful prognostic information and has relevant implications for management of TBI patients.[12,87]

In this setting, TCD may be useful as a noninvasive mean of calculating CPP. Czosnyka *et al.*[85] studied the reliability of CPP using TCD-measured CBFV in MCA (mean and diastolic) in 96 patients with TBI (Glasgow coma scale <13). The CPP measured by TCD and the calculated CPP (mean artery pressure minus ICP measured using an intraparenchymal sensor) were compared. The results showed that in 71% of the studies, the estimation error was <10 mm Hg, and in 84% of the examinations, the error was <15 mm Hg. The TCD method had a high positive predictive power (94%) for detecting low CPP (<60 mm Hg).

Although TCD can effectively noninvasively estimate ICP and CPP, avoiding the complications of invasive monitoring,[2] there are too many formulae proposed for this purpose, which show unacceptably wide CI and is not fully validated.[2,12] Hence, at present, TCD is reserved for assessing change, rather than absolute CPP, in TBI.[2]

Cerebral hypoperfusion is correlated with outcome at 6 months after TBI, so noninvasive measurement of CBF through TCD has proven to give information about prognosis similar to invasive CBF assessment.[106]

During the 72 h post-TBI, a low-flow velocity state defined as an MCA mean-CBFV of < 35 cm/s has been demonstrated to be associated with unfavorable outcome at 6 months (Glasgow outcome score [GOS] 1–3: Death, vegetative state, or severe disability).[107]

In addition, a worse outcome at 6 months (GOS 1–3) was demonstrated in 50 patients with head injury in which TCD monitoring showed VSP and hyperemia identified by insonation of the MCA, ACA, and BA in the first 7 days after traumatic brain event, respect to those without any significant flow velocity change.[108]

The highest mean-CBFV recorded, independent of VSP or hyperemia, was also predictive of outcome with those in the poor outcome group (GOS 1–3) having a significantly greater highest mean CBFV.[108]

Brain stem death is usually diagnosed by clinical examination and prolonged observation,[109] it can be confirmed with the use of ancillary diagnostic modalities such as electroencephalography (EEG), radionuclide scans, and angiography. TCD ultrasonography can be also used to support diagnosis of brain death. In addition, it may be of great value in this indication, as it is portable, less time-consuming, and can be performed at bedside. Cerebral circulatory arrest, a condition which precedes brain stem death, can be evidenced on TCD if one of following waveforms is obtained insonating BA, bilateral ICA, and bilateral MCA through two examinations at taken least 30 min apart:[110]

1. An oscillating waveform (equal systolic forward flow and diastolic reversed flow, i.e. zero net flow; or
2. Small systolic spikes of <200 ms duration and <50 cm/s PSV with no diastolic flow, or
3. Disappearance of intracranial flow with typical signals observed in the extracranial circulation.

Compared with arteriography as gold standard TCD showed a 100% agreement for the diagnosis of brain stem death.[111]

A meta-analysis performed by the AAN has demonstrated for this technique, a sensitivity and specificity range between 89% and 100% and 97% and 100%, respectively.[87,112]

Due to a certain proportion of patients having an inadequate acoustic window, the sensitivity is

unlikely to ever reach 100%, but sensitivity and specificity may improve by repeated testing. [109,111]

The consensus document of Neurosonology Research Group of the World Federation of Neurology on diagnosis of cerebral circulatory arrest using Doppler sonography confirms that extracranial and intracranial Doppler sonography is useful as a confirmatory test to establish irreversibility of cerebral circulatory arrest. Although optional, TCD is of special value when the therapeutic use of sedative drugs renders EEG unreliable.[113] This statement also mentions that the absence of flow in MCA precedes complete loss of brain stem functions. The AAN considers TCD a confirmatory test of brain death along with clinical testing and other allied tests.[114]

CONCLUSION

In NCCU, TCD examination should be routinely recommended as a noninvasive tool, which allows early identification of patients progressing to VSP secondary to aSAH and TBI.

Moreover, TCD can be used in NCCU for bedside assessment of CPP with acceptable reliability.

The frequency with which TCD should be performed may be guided by the patient clinical presentation, risk factors for VSP, and early clinical course.

The presence and temporal profile of CBFVs in all available vessels must be detected and serially monitored. The high sensitivity of TCD to identify abnormally high CBFVs due to the onset of VSP demonstrates that TCD is an excellent first-line examination to identify those patients who may need urgent aggressive treatment.

Several features of TCD assessment of VSP are similar to cerebral angiography.

Most likely, validation of new TCD criteria for VSP and combination of different physiologic monitoring modalities that includes TCD, EEG, brain tissue oxygen monitoring, cerebral microdialysis, and near-infrared spectroscopy will improve TCD accuracy to predict clinical deterioration and infarction from DCI.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Aaslid R, Markwalder TM, Nornes H. Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. *J Neurosurg.* 1982;57:769–74. [PubMed: 7143059]

2. Saqqur M, Zygun D, Demchuk A. Role of transcranial Doppler in neurocritical care. *Crit Care Med.* 2007;35(5 Suppl):S216–23. [PubMed: 17446782]

3. Rigamonti A, Ackery A, Baker AJ. Transcranial Doppler monitoring in subarachnoid hemorrhage: A critical tool in critical care. *Can J Anaesth.* 2008;55:112–23. [PubMed: 18245071]

4. Arenillas JF, Molina CA, Montaner J, Abilleira S, González-Sánchez MA, Alvarez-Sabín J. Progression and clinical recurrence of symptomatic middle cerebral artery stenosis: A long-term follow-up transcranial Doppler ultrasound study. *Stroke.* 2001;32:2898–904. [PubMed: 11739993]

5. Christou I, Felberg RA, Demchuk AM, Grotta JC, Burgin WS, Malkoff M, et al. A broad diagnostic battery for bedside transcranial Doppler to detect flow changes with internal carotid artery stenosis or occlusion. *J Neuroimaging.* 2001;11:236–42. [PubMed: 11462288]

6. Ursino M, Giulioni M. Quantitative assessment of cerebral autoregulation from transcranial Doppler pulsatility: A computer simulation study. *Med Eng Phys.* 2003;25:655–66. [PubMed: 12900181]

7. Chang JJ, Tsivgoulis G, Katsanos AH, Malkoff MD, Alexandrov AV. Diagnostic accuracy of transcranial Doppler for brain death confirmation: Systematic review and meta-analysis. *AJNR Am J Neuroradiol.* 2016;37:408–14. [PMCID: PMC7960140] [PubMed: 26514611]

8. Moreno JA, Mesalles E, Gener J, Tomasa A, Ley A, Roca J, et al. Evaluating the outcome of severe head injury with transcranial Doppler ultrasonography. *Neurosurg Focus.* 2000;8:e8. [PubMed: 16906703]

9. Pennekamp CW, Moll FL, de Borst GJ. The potential benefits and the role of cerebral monitoring in carotid endarterectomy. *Curr Opin Anaesthesiol.* 2011;24:693–7. [PubMed: 21971393]

10. Müller M, Voges M, Piepgras U, Schimrigk K. Assessment of cerebral vasomotor reactivity by transcranial Doppler ultrasound and breath-holding. A comparison with acetazolamide as vasodilatory stimulus. *Stroke.* 1995;26:96–100. [PubMed: 7839406]

11. Ringelstein EB, Droste DW, Babikian VL, Evans DH, Grosset DG, Kaps M, et al. Consensus on microembolus detection by TCD. International Consensus Group on Microembolus Detection. *Stroke.* 1998;29:725–9. [PubMed: 9506619]

12. White H, Venkatesh B. Applications of transcranial Doppler in the ICU: A review. *Intensive Care Med.* 2006;32:981–94. [PubMed: 16791661]

13. Tsivgoulis G, Alexandrov AV, Sloan MA. Advances in transcranial Doppler ultrasonography. *Curr Neurol Neurosci Rep.* 2009;9:46–54. [PubMed: 19080753]

14. Marinoni M, Ginanneschi A, Forleo P, Amaducci L. Technical limits in transcranial Doppler recording: Inadequate acoustic windows. *Ultrasound Med Biol.* 1997;23:1275–7. [PubMed: 9372576]

15. Bouzat P, Oddo M, Payen JF. Transcranial Doppler after traumatic brain injury: Is there a role? *Curr Opin Crit Care.* 2014;20:153–60. [PubMed: 24531654]

16. Paulus J, Cinotti R, Hamel O, Buffenoir K, Asehnoune K. The echographic “butterfly wing” aspect of the sphenoid bone is a critical landmark to insonate the middle cerebral artery. *Intensive Care Med.* 2014;40:1783–4. [PubMed: 25164395]

17. Aaslid R. The Doppler principle applied to measurement of blood flow velocity in cerebral arteries. In: Vienna RA,

editor. *Transcranial Doppler Sonography.* New York: Springer; 1986. pp. 22–38.

18. Tegeler CH, Crutchfield K, Katsnelson M, Kim J, Tang R, Passmore Griffin L, et al. Transcranial Doppler velocities in a large, healthy population. *J Neuroimaging.* 2013;23:466–72. [PubMed: 23157483]

19. Nicoletto HA, Burkman MH. Transcranial Doppler series part II: Performing a transcranial Doppler. *Am J Electroneurodiagnostic Technol.* 2009;49:14–27. [PubMed: 19388548]

20. Arnolds BJ, von Reutern GM. Transcranial Doppler sonography. Examination technique and normal reference values. *Ultrasound Med Biol.* 1986;12:115–23. [PubMed: 2943067]

21. Moppett IK, Mahajan RP. Transcranial Doppler ultrasonography in anaesthesia and intensive care. *Br J Anaesth.* 2004;93:710–24. [PubMed: 15220174]

22. Droste DW, Harders AG, Rastogi E. A transcranial Doppler study of blood flow velocity in the middle cerebral arteries performed at rest and during mental activities. *Stroke.* 1989;20:1005–11. [PubMed: 2667197]

23. Patel PM, Drummond JC. *Miller's Anesthesia.* 7th ed. New York: Churchill Livingstone; 2009. Cerebral physiology and the effects of anesthetic drugs; pp. 305–40.

24. Shahlaie K, Keachie K, Hutchins IM, Rudisill N, Madden LK, Smith KA, et al. Risk factors for posttraumatic vasospasm. *J Neurosurg.* 2011;115:602–11. [PubMed: 21663415]

25. Kaps M, Stolz E, Allendoerfer J. Prognostic value of transcranial sonography in acute stroke patients. *Eur Neurol.* 2008;59(Suppl 1):9–16. [PubMed: 18382108]

26. Carrera E, Schmidt JM, Oddo M, Fernandez L, Claassen J, Seder D, et al. Transcranial Doppler for predicting delayed cerebral ischemia after subarachnoid hemorrhage. *Neurosurgery.* 2009;65:316–23. [PubMed: 19625911]

27. Brauer P, Kochs E, Werner C, Bloom M, Policare R, Pentheny S, et al. Correlation of transcranial Doppler sonography mean flow velocity with cerebral blood flow in patients with intracranial pathology. *J Neurosurg Anesthesiol.* 1998;10:80–5. [PubMed: 9559765]

28. Gosling RG, King DH. Arterial assessment by Doppler-shift ultrasound. *Proc R Soc Med.* 1974;67(6 Pt 1):447–9. [PMCID: PMC1645777] [PubMed: 4850636]

29. Nicoletto HA, Burkman MH. Transcranial Doppler series part III: Interpretation. *Am J Electroneurodiagnostic Technol.* 2009;49:244–59. [PubMed: 19891416]

30. Homburg AM, Jakobsen M, Enevoldsen E. Transcranial Doppler recordings in raised intracranial pressure. *Acta Neurol Scand.* 1993;87:488–93. [PubMed: 8356880]

31. Bellner J, Romner B, Reinstrup P, Kristiansson KA, Ryding E, Brandt L. Transcranial Doppler sonography pulsatility index (PI) reflects intracranial pressure (ICP) *Surg Neurol.* 2004;62:45–51. [PubMed: 15226070]

32. Ursino M, Giulioni M, Lodi CA. Relationships among cerebral perfusion pressure, autoregulation, and transcranial Doppler waveform: A modeling study. *J Neurosurg.* 1998;89:255–66. [PubMed: 9688121]

33. Zweifel C, Czosnyka M, Carrera E, de Riva N, Pickard JD, Smielewski P. Reliability of the blood flow velocity pulsatility index for assessment of intracranial and cerebral perfusion pressures in head-injured patients. *Neurosurgery.* 2012;71:853–61. [PubMed: 22791038]

34. Lindegaard KF, Nornes H, Bakke SJ, Sorteberg W, Nakstad P. Cerebral vasospasm after subarachnoid haemorrhage

investigated by means of transcranial Doppler ultrasound. *Acta Neurochir Suppl (Wien)* 1988;42:81–4. [PubMed: 3055838]

35. Martin PJ, Evans DH, Naylor AR. Transcranial color-coded sonography of the basal cerebral circulation. Reference data from 115 volunteers. *Stroke.* 1994;25:390–6. [PubMed: 7905680]

36. Rasulo FA, De Peri E, Lavinio A. Transcranial Doppler ultrasonography in intensive care. *Eur J Anaesthesiol Suppl.* 2008;42:167–73. [PubMed: 18289437]

37. Krejza J, Mariak Z, Walecki J, Szydlik P, Lewko J, Ustymowicz A. Transcranial color Doppler sonography of basal cerebral arteries in 182 healthy subjects: Age and sex variability and normal reference values for blood flow parameters. *AJR Am J Roentgenol.* 1999;172:213–8. [PubMed: 9888770]

38. Maeda H, Matsumoto M, Handa N, Hougaku H, Ogawa S, Itoh T, et al. Reactivity of cerebral blood flow to carbon dioxide in various types of ischemic cerebrovascular disease: Evaluation by the transcranial Doppler method. *Stroke.* 1993;24:670–5. [PubMed: 8488521]

39. Velat GJ, Kimball MM, Mocco JD, Hoh BL. Vasospasm after aneurysmal subarachnoid hemorrhage: Review of randomized controlled trials and metaanalyses in the literature. *World Neurosurg.* 2011;76:446–54. [PubMed: 22152574]

40. Dorsch N. A clinical review of cerebral vasospasm and delayed ischaemia following aneurysm rupture. *Acta Neurochir Suppl.* 2011;110(Pt 1):5–6. [PubMed: 21116906]

41. Papaioannou V, Dragoumanis C, Theodorou V, Konstantonis D, Pneumatikos I, Birbilis T. Transcranial Doppler ultrasonography in intensive care unit. Report of a case with subarachnoid hemorrhage and brain death and review of the literature. *Greek E J Perioper Med.* 2008;6:95–104.

42. Biller J, Godersky JC, Adams HP., Jr Management of aneurysmal subarachnoid hemorrhage. *Stroke.* 1988;19:1300–5. [PubMed: 3176090]

43. Zubkov AY, Rabinstein AA. Medical management of cerebral vasospasm: Present and future. *Neurol Res.* 2009;31:626–31. [PubMed: 19055879]

44. Smith M. Intensive care management of patients with subarachnoid haemorrhage. *Curr Opin Anaesthesiol.* 2007;20:400–7. [PubMed: 17873592]

45. Dorsch NW, King MT. A review of cerebral vasospasm in aneurysmal subarachnoid haemorrhage Part I: Incidence and effects. *J Clin Neurosci.* 1994;1:19–26. [PubMed: 18638721]

46. Mascia L, Fedorko L, terBrugge K, Filippini C, Pizzio M, Ranieri VM, et al. The accuracy of transcranial Doppler to detect vasospasm in patients with aneurysmal subarachnoid hemorrhage. *Intensive Care Med.* 2003;29:1088–94. [PubMed: 12774157]

47. Otten ML, Mocco J, Connolly ES, Jr, Solomon RA. A review of medical treatments of cerebral vasospasm. *Neurol Res.* 2008;30:444–9. [PubMed: 18953733]

48. Marshall SA, Nyquist P, Ziai WC. The role of transcranial Doppler ultrasonography in the diagnosis and management of vasospasm after aneurysmal subarachnoid hemorrhage. *Neurosurg Clin N Am.* 2010;21:291–303. [PubMed: 20380971]

49. Harders AG, Gilsbach JM. Time course of blood velocity changes related to vasospasm in the circle of Willis measured

by transcranial Doppler ultrasound. *J Neurosurg.* 1987;66:718–28. [PubMed: 3553456]

50. Armonda RA, Bell RS, Vo AH, Ling G, DeGraba TJ, Crandall B, et al. Wartime traumatic cerebral vasospasm: Recent review of combat casualties. *Neurosurgery.* 2006;59:1215–25. [PubMed: 17277684]

51. Keyrouz SG, Diringer MN. Clinical review: Prevention and therapy of vasospasm in subarachnoid hemorrhage. *Crit Care.* 2007;11:220. [PMCID: PMC2206512] [PubMed: 17705883]

52. Topcuoglu MA, Pryor JC, Ogilvy CS, Kistler JP. Cerebral vasospasm following subarachnoid hemorrhage. *Curr Treat Options Cardiovasc Med.* 2002;4:373–384. [PubMed: 12194810]

53. Sviri GE, Ghodke B, Britz GW, Douville CM, Haynor DR, Mesiwala AH, et al. Transcranial Doppler grading criteria for basilar artery vasospasm. *Neurosurgery.* 2006;59:360–6. [PubMed: 16883176]

54. Bederson JB, Connolly ES, Jr, Batjer HH, Dacey RG, Dion JE, Diringer MN, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke.* 2009;40:994–1025. [PubMed: 19164800]

55. McGirt MJ, Blessing RP, Goldstein LB. Transcranial Doppler monitoring and clinical decision-making after subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis.* 2003;12:88–92. [PubMed: 17903910]

56. Washington CW, Zipfel GJ. Participants in the International Multi-disciplinary Consensus Conference on the Critical Care Management of Subarachnoid Hemorrhage. Detection and monitoring of vasospasm and delayed cerebral ischemia: A review and assessment of the literature. *Neurocrit Care.* 2011;15:312–7. [PubMed: 21748499]

57. Lysakowski C, Walder B, Costanza MC, Tramèr MR. Transcranial Doppler versus angiography in patients with vasospasm due to a ruptured cerebral aneurysm: A systematic review. *Stroke.* 2001;32:2292–8. [PubMed: 11588316]

58. Vora YY, Suarez-Almazor M, Steinke DE, Martin ML, Findlay JM. Role of transcranial Doppler monitoring in the diagnosis of cerebral vasospasm after subarachnoid haemorrhage. *Neurosurgery.* 1999;44:1237–47. [PubMed: 10371622]

59. Schatlo B, Pluta RM. Clinical applications of transcranial Doppler sonography. *Rev Recent Clin Trials.* 2007;2:49–57. [PubMed: 18473988]

60. Sloan MA, Burch CM, Wozniak MA, Rothman MI, Rigamonti D, Permutt T, et al. Transcranial Doppler detection of vertebrobasilar vasospasm following subarachnoid hemorrhage. *Stroke.* 1994;25:2187–97. [PubMed: 7974544]

61. Soustiel JF, Shik V, Shreiber R, Tavor Y, Goldsher D. Basilar vasospasm diagnosis: Investigation of a modified "Lindegaard Index" based on imaging studies and blood velocity measurements of the basilar artery. *Stroke.* 2002;33:72–7. [PubMed: 11779892]

62. Harders A, Gilsbach J. Transcranial Doppler sonography and its application in extracranial-intracranial bypass surgery. *Neurol Res.* 1985;7:129–41. [PubMed: 2866457]

63. Skjelland M, Krohg-Sørensen K, Tennøe B, Bakke SJ, Brucher R, Russell D. Cerebral microemboli and brain injury during carotid artery endarterectomy and stenting. *Stroke.* 2009;40:230–4. [PubMed: 18927460]

64. Wozniak MA, Sloan MA, Rothman MI, Burch CM, Rigamonti D, Permutt T, et al. Detection of vasospasm by transcranial Doppler sonography. The challenges of the anterior and posterior cerebral arteries. *J Neuroimaging.* 1996;6:87–93. [PubMed: 8634493]

65. Frontera JA, Fernandez A, Schmidt JM, Claassen J, Wartenberg KE, Badjatia N, et al. Defining vasospasm after

subarachnoid hemorrhage: What is the most clinically relevant definition? *Stroke.* 2009;40:1963–8. [PubMed: 19359629]

66. Gonzalez NR, Boscardin WJ, Glenn T, Vinuela F, Martin NA. Vasospasm probability index: A combination of transcranial Doppler velocities, cerebral blood flow, and clinical risk factors to predict cerebral vasospasm after aneurysmal subarachnoid hemorrhage. *J Neurosurg.* 2007;107:1101–12. [PubMed: 18077946]

67. Connolly ES, Jr, Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida RT, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2012;43:1711–37. [PubMed: 22556195]

68. Puppo C, López L, Caragna E, Biestro A. One-minute dynamic cerebral autoregulation in severe head injury patients and its comparison with static autoregulation. A transcranial Doppler study. *Neurocrit Care.* 2008;8:344–52. [PubMed: 18363042]

69. Aries MJ, Elting JW, De Keyser J, Kremer BP, Vroomen PC. Cerebral autoregulation in stroke: A review of transcranial Doppler studies. *Stroke.* 2010;41:2697–704. [PubMed: 20930158]

70. Reinhard M, Roth M, Müller T, Czosnyka M, Timmer J, Hetzel A. Cerebral autoregulation in carotid artery occlusive disease assessed from spontaneous blood pressure fluctuations by the correlation coefficient index. *Stroke.* 2003;34:2138–44. [PubMed: 12920261]

71. Panerai RB. Transcranial Doppler for evaluation of cerebral autoregulation. *Clin Auton Res.* 2009;19:197–211. [PubMed: 19370374]

72. Panerai RB. Assessment of cerebral pressure autoregulation in humans - A review of measurement methods. *Physiol Meas.* 1998;19:305–38. [PubMed: 9735883]

73. Paulson OB, Strandgaard S, Edvinsson L. Cerebral autoregulation. *Cerebrovasc Brain Metab Rev.* 1990;2:161–92. [PubMed: 2201348]

74. Aaslid R, Lindegaard KF, Sorteberg W, Nornes H. Cerebral autoregulation dynamics in humans. *Stroke.* 1989;20:45–52. [PubMed: 2492126]

75. Giller CA. A bedside test for cerebral autoregulation using transcranial Doppler ultrasound. *Acta Neurochir (Wien)* 1991;108:7–14. [PubMed: 2058430]

76. Tiecks FP, Douville C, Byrd S, Lam AM, Newell DW. Evaluation of impaired cerebral autoregulation by the valsalva maneuver. *Stroke.* 1996;27:1177–82. [PubMed: 8685924]

77. Schondorf R, Stein R, Roberts R, Benoit J, Cupples W. Dynamic cerebral autoregulation is preserved in neurally mediated syncope. *J Appl Physiol.* 2001;91:2493–502. [PubMed: 11717210]

78. Levine BD, Giller CA, Lane LD, Buckey JC, Blomqvist CG. Cerebral versus systemic hemodynamics during graded orthostatic stress in humans. *Circulation.* 1994;90:298–306. [PubMed: 8026012]

79. Tiecks FP, Lam AM, Aaslid R, Newell DW. Comparison of static and dynamic cerebral autoregulation measurements. *Stroke.* 1995;26:1014–9. [PubMed: 7762016]

80. Czosnyka M, Brady K, Reinhard M, Smielewski P, Steiner LA. Monitoring of cerebrovascular autoregulation: Facts, myths, and missing links. *Neurocrit Care.* 2009;10:373–86. [PubMed: 19127448]

81. Panerai RB. Cerebral autoregulation: From models to clinical applications. *Cardiovasc Eng.* 2008;8:42–59. [PubMed:

18041584]

82. Czosnyka M, Smielewski P, Kirkpatrick P, Menon DK, Pickard JD. Monitoring of cerebral autoregulation in head-injured patients. *Stroke.* 1996;27:1829–34. [PubMed: 8841340]

83. Lang EW, Diehl RR, Mehdorn HM. Cerebral autoregulation testing after aneurysmal subarachnoid hemorrhage: The phase relationship between arterial blood pressure and cerebral blood flow velocity. *Crit Care Med.* 2001;29:158–63. [PubMed: 11176177]

84. White RP, Markus HS. Impaired dynamic cerebral autoregulation in carotid artery stenosis. *Stroke.* 1997;28:1340–4. [PubMed: 9227680]

85. Czosnyka M, Matta BF, Smielewski P, Kirkpatrick PJ, Pickard JD. Cerebral perfusion pressure in head-injured patients: A noninvasive assessment using transcranial Doppler ultrasonography. *J Neurosurg.* 1998;88:802–8. [PubMed: 9576246]

86. Clark JM, Skolnick BE, Gelfand R, Farber RE, Stierheim M, Stevens WC, et al. Relationship of 133Xe cerebral blood flow to middle cerebral arterial flow velocity in men at rest. *J Cereb Blood Flow Metab.* 1996;16:1255–62. [PubMed: 8898699]

87. Sloan MA, Alexandrov AV, Tegeler CH, Spencer MP, Caplan LR, Feldmann E, et al. Assessment: Transcranial Doppler ultrasonography: Report of the therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology.* 2004;62:1468–81. [PubMed: 15136667]

88. Demchuk AM, Christou I, Wein TH, Felberg RA, Malkoff M, Grotta JC, et al. Accuracy and criteria for localizing arterial occlusion with transcranial Doppler. *J Neuroimaging.* 2000;10:1–12. [PubMed: 10666975]

89. Razumovsky AY, Gillard JH, Bryan RN, Hanley DF, Oppenheimer SM. TCD, MRA and MRI in acute cerebral ischemia. *Acta Neurol Scand.* 1999;99:65–76. [PubMed: 9925241]

90. Tsivgoulis G, Sharma VK, Lao AY, Malkoff MD, Alexandrov AV. Validation of transcranial Doppler with computed tomography angiography in acute cerebral ischemia. *Stroke.* 2007;38:1245–9. [PubMed: 17332465]

91. Camerlingo M, Casto L, Censori B, Servalli MC, Ferraro B, Mamoli A. Prognostic use of ultrasonography in acute non-hemorrhagic carotid stroke. *Ital J Neurol Sci.* 1996;17:215–8. [PubMed: 8856412]

92. Baracchini C, Manara R, Ermani M, Meneghetti G. The quest for early predictors of stroke evolution: Can TCD be a guiding light? *Stroke.* 2000;31:2942–7. [PubMed: 11108753]

93. Kushner MJ, Zanette EM, Bastianello S, Mancini G, Sacchetti ML, Carolei A, et al. Transcranial Doppler in acute hemispheric brain infarction. *Neurology.* 1991;41:109–13. [PubMed: 1985274]

94. Demchuk AM, Burgin WS, Christou I, Felberg RA, Barber PA, Hill MD, et al. Thrombolysis in brain ischemia (TIBI) transcranial Doppler flow grades predict clinical severity, early recovery, and mortality in patients treated with intravenous tissue plasminogen activator. *Stroke.* 2001;32:89–93. [PubMed: 11136920]

95. Christou I, Alexandrov AV, Burgin WS, Wojner AW, Felberg RA, Malkoff M, et al. Timing of recanalization after tissue plasminogen activator therapy determined by transcranial Doppler correlates with clinical recovery from ischemic stroke. *Stroke.* 2000;31:1812–6. [PubMed: 10926939]

96. Alexandrov AV, Burgin WS, Demchuk AM, El-Mitwalli A, Grotta JC. Speed of intracranial clot lysis with intravenous tissue plasminogen activator therapy: Sonographic classification and short-term improvement. *Circulation.* 2001;103:2897–902. [PubMed: 11413077]

97. Alexandrov AV, Grotta JC. Arterial reocclusion in stroke patients treated with intravenous tissue plasminogen

activator. *Neurology.* 2002;59:862–7. [PubMed: 12297567]

98. Stolz E, Cioli F, Allendoerfer J, Gerriets T, Del Sette M, Kaps M. Can early neurosonology predict outcome in acute stroke? a metaanalysis of prognostic clinical effect sizes related to the vascular status. *Stroke.* 2008;39:3255–61. [PubMed: 18845799]

99. Jauch EC, Saver JL, Adams HP, Jr, Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2013;44:870–947. [PubMed: 23370205]

100. Platt OS. Prevention and management of stroke in sickle cell anemia. *Hematology Am Soc Hematol Educ Program.* 2006:54–7. [PubMed: 17124040]

101. Adams RJ, McKie VC, Carl EM, Nichols FT, Perry R, Brock K, et al. Long-term stroke risk in children with sickle cell disease screened with transcranial Doppler. *Ann Neurol.* 1997;42:699–704. [PubMed: 9392568]

102. Adams RJ, McKie VC, Hsu L, Files B, Vichinsky E, Pegelow C, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. *N Engl J Med.* 1998;339:5–11. [PubMed: 9647873]

103. Adams RJ. TCD in sickle cell disease: An important and useful test. *Pediatr Radiol.* 2005;35:229–34. [PubMed: 15703904]

104. Werner C, Engelhard K. Pathophysiology of traumatic brain injury. *Br J Anaesth.* 2007;99:4–9. [PubMed: 17573392]

105. Martin NA, Patwardhan RV, Alexander MJ, Africk CZ, Lee JH, Shalmon E, et al. Characterization of cerebral hemodynamic phases following severe head trauma: Hypoperfusion, hyperemia, and vasospasm. *J Neurosurg.* 1997;87:9–19. [PubMed: 9202259]

106. Jaggi JL, Obrist WD, Gennarelli TA, Langfitt TW. Relationship of early cerebral blood flow and metabolism to outcome in acute head injury. *J Neurosurg.* 1990;72:176–82. [PubMed: 2295915]

107. van Santbrink H, Schouten JW, Steyerberg EW, Avezaat CJ, Maas AI. Serial transcranial Doppler measurements in traumatic brain injury with special focus on the early posttraumatic period. *Acta Neurochir (Wien)* 2002;144:1141–9. [PubMed: 12434170]

108. Zurynski YA, Dorsch NW, Fearnside MR. Incidence and effects of increased cerebral blood flow velocity after severe head injury: A transcranial Doppler ultrasound study II. Effect of vasospasm and hyperemia on outcome. *J Neurol Sci.* 1995;134:41–6. [PubMed: 8747841]

109. Llompart-Pou JA, Abadal JM, Güenther A, Rayo L, Martín-del Rincón JP, Homar J, et al. Transcranial sonography and cerebral circulatory arrest in adults: A comprehensive review. *ISRN Crit Care.* 2013:1–6. Doi: http://dx.doi.org/10.5402/2013/167468.

110. Ducrocq X, Braun M, Debouverie M, Junges C, Hummer M, Vespignani H. Brain death and transcranial Doppler: Experience in 130 cases of brain dead patients. *J Neurol Sci.* 1998;160:41–6. [PubMed: 9804115]

111. Poularas J, Karakitsos D, Kouraklis G, Kostakis A, De Groot E, Kalogeromitros A, et al. Comparison between transcranial color Doppler ultrasonography and angiography in the confirmation of brain death. *Transplant Proc.* 2006;38:1213–7. [PubMed: 16797266]

112. Monteiro LM, Bollen CW, van Huffelen AC, Ackerstaff RG, Jansen NJ, van Vught AJ. Transcranial Doppler

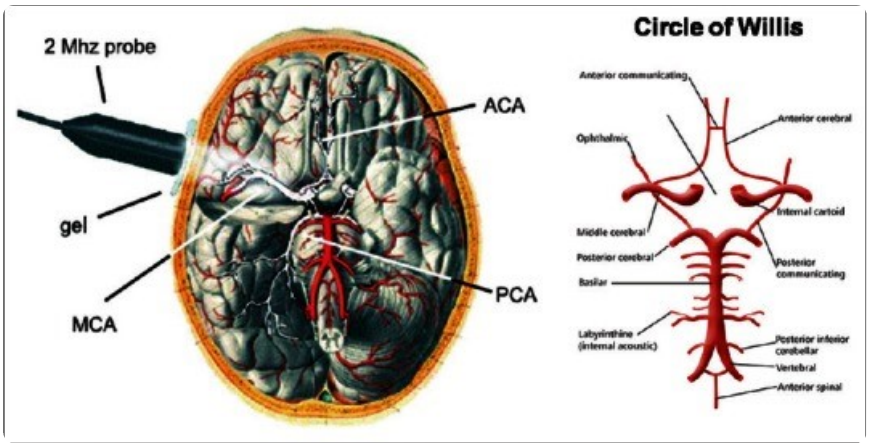
ultrasonography to confirm brain death: A meta-analysis. *Intensive Care Med.* 2006;32:1937–44. [PubMed: 17019556]

113. Ducrocq X, Hassler W, Moritake K, Newell DW, von Reutern GM, Shiogai T, et al. Consensus opinion on diagnosis of cerebral circulatory arrest using Doppler-sonography: Task Force Group on cerebral death of the Neurosonology Research Group of the World Federation of Neurology. *J Neurol Sci.* 1998;159:145–50. [PubMed: 9741398]

114. Wijdicks EF. Determining brain death in adults. *Neurology.* 1995;45:1003–11. [PubMed: 7746373]

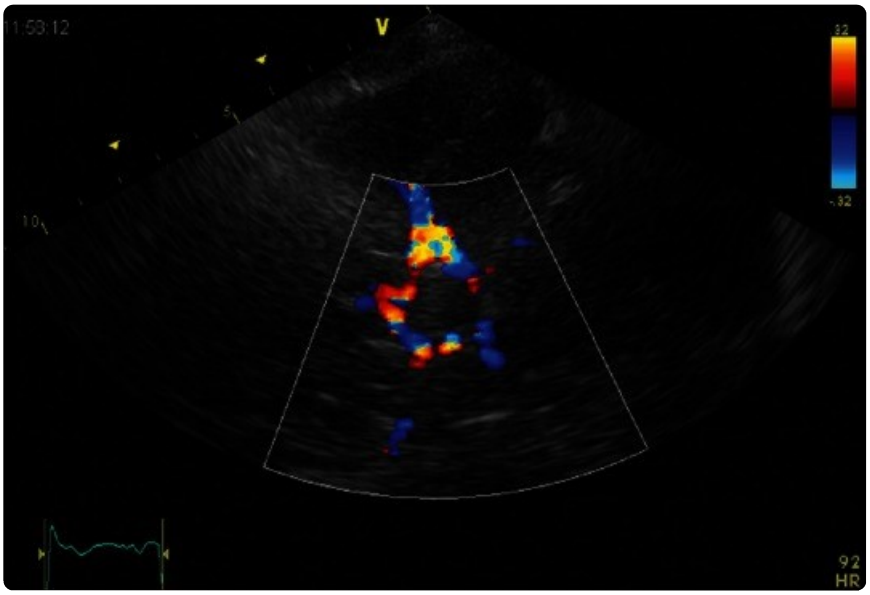
Figures and Tables

Figure 1



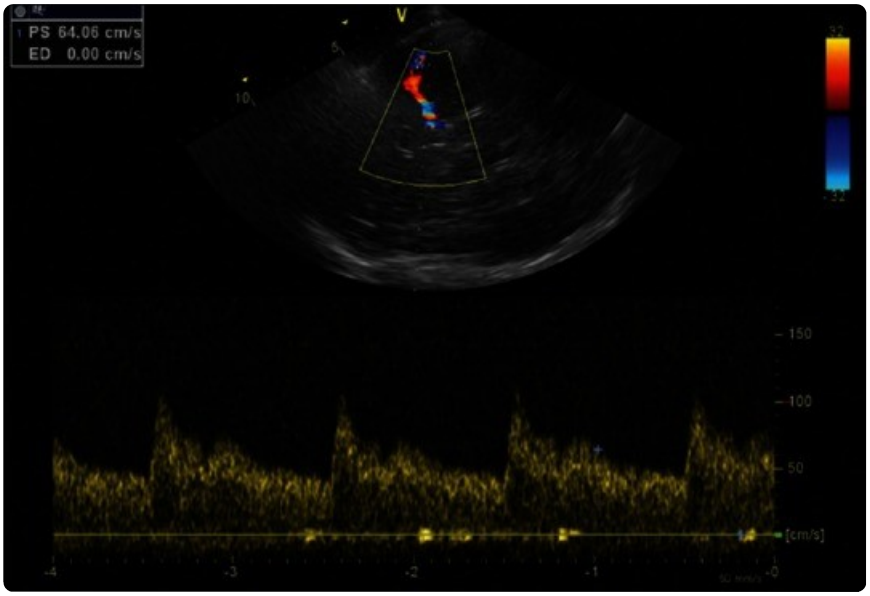
Left panel: Transmission of ultrasound beam through skull using Pulsed Doppler sectorial probe with a 2.0–3.5 MHz emission frequency. Probe is positioned on temporal window. Right panel = Circle of Willis

Figure 2



Mesencephalic view. It is clearly distinguishable the middle cerebral artery

Figure 3



Transcranial Doppler spectral Doppler study of intracranial middle cerebral artery. MCA = Middle cerebral artery

Table 1a

Factors influencing cerebral blood flow velocity

Factor	Change in CBFV
Age	Increase up 6-10 years then decrease
Sex	Women > men
Pregnancy	Decrement in the third trimester
Hematocrit	Increase with decreasing hematocrit
PCO_2	Increase with increasing PCO_2
MAP	Increase with increasing MAP

MAP=Main arterial pressure, PCO_2=Pressure of oxygen, CBFV=Cerebral blood flow velocity

Table 1b

Mean cerebral blood flow velocity (cm/s) related to age

Artery	Age 20-40 years	Age 40-60 years	Age >60 years
Anterior cerebral artery	56-60	53-61	44-51
MCA	74-81	72-73	58-59
PCA			
P1	48-57	41-56	37-47
P2	43-51	40-57	37-47
Vertebral artery	37-51	29-50	30-37
Basilar artery	39-58	27-56	29-47

MCA=Middle cerebral artery, PCA=Posterior cerebral artery

Table 2

Pulsatility index and resistivity index indices: Changes and conditions related

Elevated PI/RI	Decreased PI/RI
Increased ICP	Vasospasm/hyperemia
Hydrocephalus	AV malformation
Fulminant hepatic failure	
Bacterial meningitis	
Encephalopathy	
Brain death	

PI=Pulsatility index, RI=Resistivity index, ICP=Intracranial pressure, AV=Arteriovenous

Table 3

Intracranial arteries: Severity of vasospasm

	MFV (cm/s)	LR modified
MCA or ICA vasospasm (%)		
Mild (<25)	120-149	3-6
Moderate (25-50)	150-199	3-6
Severe (>50)	>200	>6
BA vasospasm (%)		
Possible vasospasm	70-85	2-2.49
Moderate (25-50)	>85	2.5-2.99
Severe (>50)	>85	>3

ICA=Internal carotid artery, MCA=Middle cerebral artery, MFV=Mean flow velocity, BA=Basilar artery, LR=Lindegaard ratio