Transcranial Doppler and Transcranial Color-Coded Duplex Sonography

24

Chiara Robba and Andrea Rigamonti

24.1 Basic Principles of Transcranial Doppler

Transcranial Doppler (TCD) ultrasonography was first described by Aaslid and collaborators in 1982 [1]. It is a noninvasive technique able to monitor dynamics of cerebral blood flow (CBF) and vessel pulsatility in the basal cerebral arteries, such as middle cerebral artery (MCA), anterior cerebral artery (ACA), and posterior cerebral artery (PCA) (Fig. 24.1).

TCD technique is based on the phenomenon described by the physicist Christian Andreas Doppler in the nineteenth century, called Doppler Effect. According to this principle, when a sound wave with a certain frequency strikes a moving object (such as red blood cell inside an insonated artery), it is reflected with a different frequency, the Doppler shift, fd, which is directly proportional to the velocity of the object (V). Echoes received by the ultrasound (US) probe are processed to produce a spectral waveform with peak systolic velocity and diastolic velocity values (Fig. 24.2).

$$V = \frac{(c \times fd)}{2 \times f0 \times \cos\theta}$$

(c is the speed of the incident wave, $f0$ is the incident pulse frequency, and θ is the angle of the reflector relative to the US probe).

The spectral waveform is then processed and combined with indices derived from cerebral blood flow velocity (FV) (such as Gosling's and spectral pulsatility index) allowing the calculation of secondary indices (including autoregulation, critical closing pressure (CrCP), noninvasive intracranial pressure [ICP]) useful for the analysis of cerebral hemodynamics.

The main obstacle to vessel insonation and ultrasound penetration of the skull is the bone. Therefore, TCD is performed through acoustic windows representing specific points of the skull where the bone is thin enough to allow ultrasound waves to penetrate.

The equipment used is a duplex US color flow mapper. The probe is either a sector or phased array cardiac or dedicated probe with a small imaging footprint and a Doppler frequency of 1.8 or 2 MHz.

C. Robba (✉)
Neurocritical Care Unit, Addenbrookes Hospital, Cambridge, UK
e-mail: kiarobba@gmail.com

A. Rigamonti
Departments of Anaesthesia and Critical Care, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada
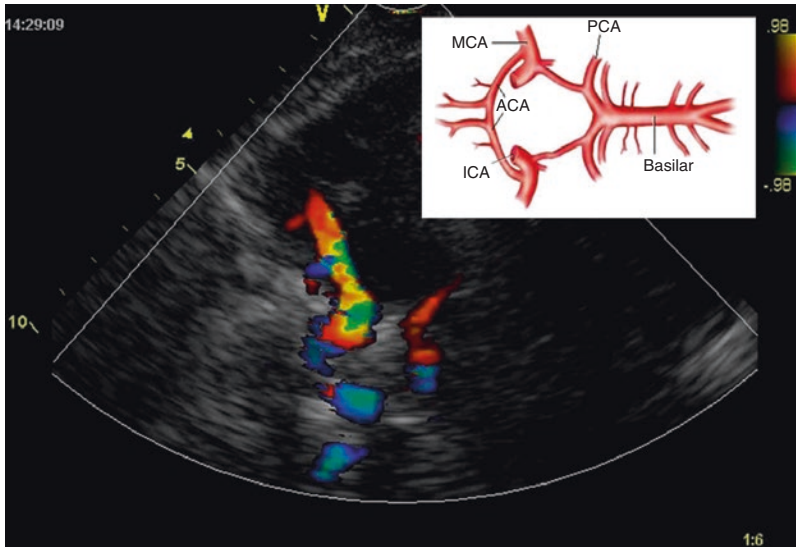
Fig. 24.1 Typical transcranial color-coded duplex sonography (TCCS) view of the circle of Willis
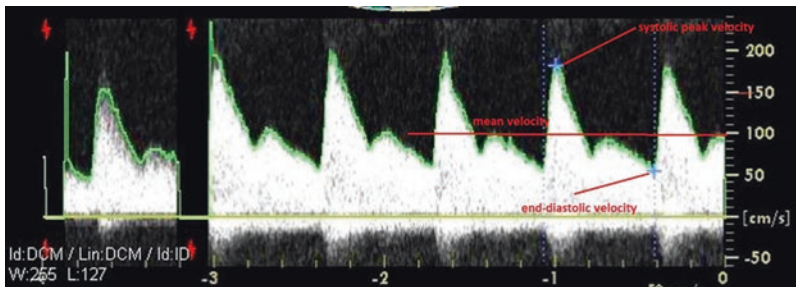

Fig. 24.2 Spectral waveform highlighting the peak systolic and the diastolic velocity values

24.2   Acoustic Windows

The acoustic windows used to insonate the vessels are transtemporal, suboccipital, transorbital, and retromandibular (Fig. 24.3). The temporal window is the most commonly used for the insonation of the MCA (responsible for the 75% of the brain blood flow and it is the vessel of choice for most of the TCD derived signals), ACA, and PCA (Fig. 24.4). The posterior circulation, in particular terminal segments of the vertebral and basilar arteries, can be visualized via the suboccipital (transforaminal) window. Transorbital examination allows the insonation of the ophthalmic arteries and carotid siphons, as well as the measurement of

the optic nerve sheath diameters [2]. In patients with subarachnoid hemorrhage (SAH) and suspect of vasospasm, a submandibular approach can be used to insonate the extracranial portion of the internal carotid artery (ICA) to calculate the mean flow velocity ratio between the MCA and ICA (Lindegaard index). Finally, in newborns, open fontanelles provide a good acoustic window to the intracranial circulation; internal carotid vessels and the branches of the circle of Willis can be insonated through the anterior fontanelle in sagittal and coronal planes [3].

The identification of each intracranial vessel is based on the depth of signal capture, velocity and direction of the vessel, possibility of following

Fig. 24.3 Transtemporal and suboccipital (or transforaminal) windows and vascular cerebral anatomy (Courtesy of Maria Blouin)
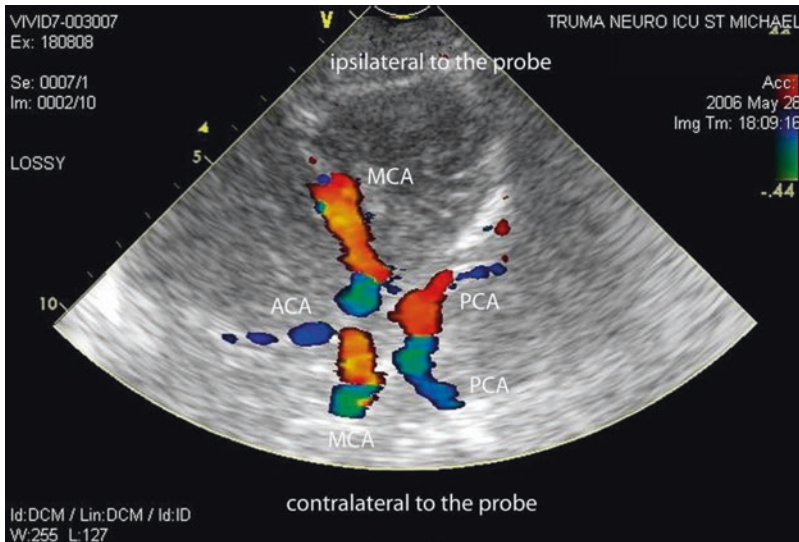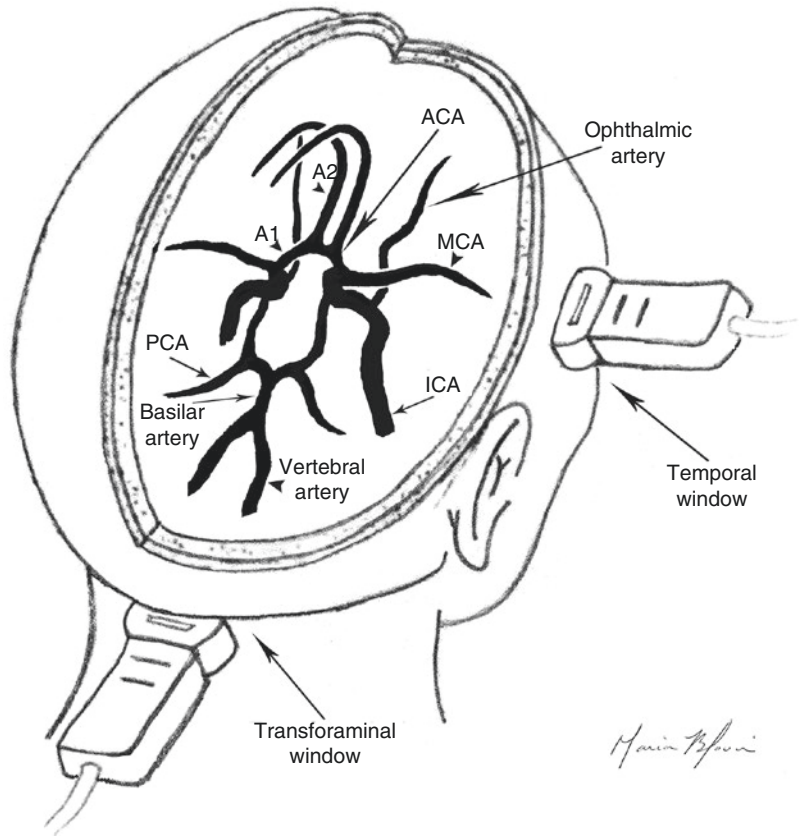

Fig. 24.4 Typical view through the temporal window

Table 24.1 Normal values of flow velocities of the main cerebral vessels detected by transcranial doppler in adults

	Acoustic window	Mean FV (cm/s)	Depth (mm)	Direction of flow
MCA	Transtemporal	55 ± 12	30–65	Toward
ACA	Transtemporal	50 ± 11	60–75	Away
PCA	Transtemporal	40 ± 10	60–70	Toward (P1), Away (P2)
BA	Occipital	41 ± 10	80–120	Away
VA	Occipital	38 ± 10	60–75	Away
OA	Transorbital	21 ± 5	45–55	Toward
ICA	Retromandibular	30 ± 9	45–50	Away

Abbreviations: MCA middle cerebral artery, *ACA* anterior cerebral artery, *PCA* posterior cerebral artery, *BA* basilar artery, *VA* vertebral artery, *OA* ophthalmic artery, *ICA* internal carotid artery

Fig. 24.5 Systolic (FVs), diastolic (FVd), and mean (FVm) flow velocities generated by spectral analysis
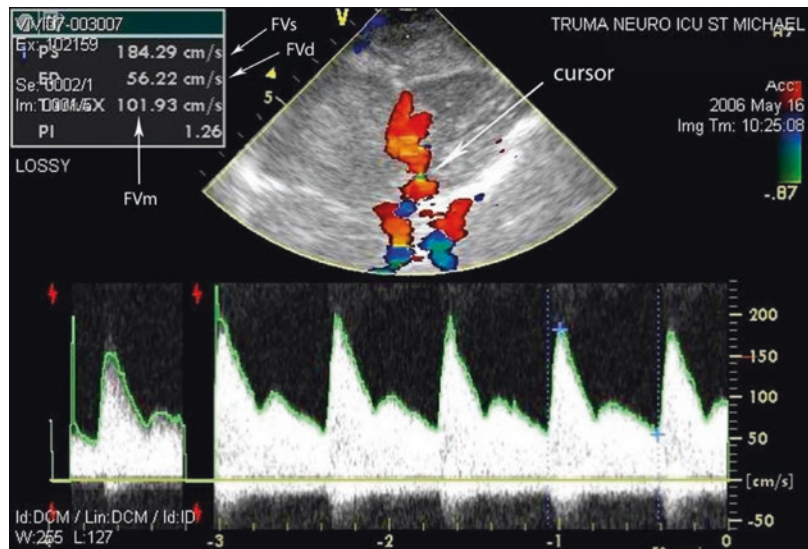
the vessel its whole length and anatomical relationship with other vessels (Table 24.1).

Transcranial color-duplex sonography (TCCS) combines pulsed-wave Doppler with two-dimensional, real-time B mode imaging. It allows the direct visualization of basal cerebral arteries anatomy; therefore, it allows precise placement of the Doppler sample volume in the vessel. Compared to conventional TCD, TCCS is more reliable and accurate.

24.3   TCD-Derived Signals

The processing of the echoes received by the US probe produces a spectral waveform. Systolic (FVs), diastolic (FVd), and mean (FVm) flow velocities will be then generated by the analysis of the waveform (Fig. 24.5).

Pulsatility index (PI) is a TCD-derived parameter able to provide information about cerebral vascular resistance and changes in the morphology of the TCD waveform resulting from cerebral perfusion pressure (CPP) changes.

Mathematically, PI is calculated as the relationship between the difference of FVs and FVd divided by mean flow velocity (FVm) [4] (Figs. 24.6 and 24.7)

$$PI = \frac{FVs - FVd}{FVm}$$

PI has been widely investigated as noninvasive estimator of ICP. Some authors demonstrated that ICP and PI are positively correlated during

Fig. 24.6 Pulsatility index (PI) and resistivity index (RI)
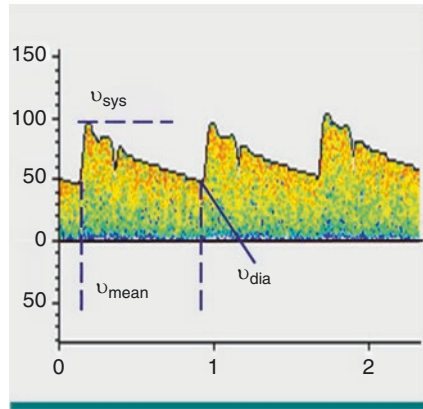
Pulsatility index (gosling)

$$PI = \frac{FV_s - FV_d}{FV_m}$$

Resistivity index (pourcelot)

$$PI = \frac{FV_s - FV_d}{FV_m}$$

Both indices tend to increase with age

Fig. 24.7 Normal and abnormal PI

Pulsatility index

- **PI < 0.5 – Below normal resistance**
  May suggest a proximal narrowing / occlusin or an artero-venous malformation

- **0.5 < PI < 1.0 – Normal resistance**

- **1.1 < PI < 1.5 – Above normal resistance**

- **PI > 1.5 – Abnormal resistance**
  PIs > 1.1 may be caused by a distal occlusion.When blood flow hits the occlusion it causes flow to stop abruptly. The result is a decrease in diastolic flow or a reversal of flow in early diastole and little or no flow in late diastole. Arterial constriction 9i.e. vasospasm) will also cause PL to elevate

increases of ICP [5], demonstrating a strong correlation coefficient with invasively measured ICP ($R = 0.94$ $p < 0.05$) [6]. However, other authors found less positive results finding a weak correlation between PI and ICP [6, 7]. However, PI is not specific for increase in ICP. When a drop in CPP occurs, PI presents an increasing trend, which can be related to increases in ICP but also to decreases in cerebrovascular resistance (CVR). Similarly, during hypocapnia, both CVR and PI increase significantly [8]. Many studies have supported the idea that PI can reflect distal CVR, attributing greater PI to higher CVR [9].

However, experimental data showed that hypercapnia can cause a decrease in both CVR and PI while a reduction in CPP with intact autoregulation induces a decrease in CVR but an increase in PI [10]; therefore, PI is dependent on numerous factors, including ICP, ABP, on CPP and vascular tone (consequently CO_2).

In summary, changes in PI are correlated to changes both in ICP and ABP. Although a few manuscripts favor PI as a surrogate ICP, the sensitivity of PI to identify raised ICP is high, but its specificity is low.

24.4 Cerebral Blood Flow

Under normal conditions, FV is proportional to the cerebral blood flow (CBF). Although TCD is not appropriate to yield an absolute value of CBF, changes over time in FV are related to changes in CBF. Therefore, since TCD gives a quantitative

measurement of FVs, the measurement of changes in FV provides a quantitative measurement of changes in CBF.

TCD-derived cerebral blood FVs are commonly measured in clinical and experimental environment. The simultaneous monitoring of these signals as well as intracranial pressure (ICP) and arterial blood pressure (ABP) can give valuable information regarding the state of cerebral hemodynamics in different intracranial pathologies. Through the analysis of TCD waveform, many authors attempted to investigate the relationship between the cerebral blood flow (CBF) and cerebrospinal fluid (CSF) dynamics, proposing several mathematical and hydrodynamic models [12–14].

24.5   Anesthetic Agents and Intracranial Blood Flow Velocity

24.5.1 Volatile Agents

Cerebral vasodilatory effects of volatile agents have been extensively studied [11]; according to most authors, the vasodilatory effect of volatile agents on cerebral vessels is dose dependent and less evident with sevoflurane when compared with other inhalational agents [12]. Conversely, propofol is not associated with a significant modification of cerebral hemodynamics and demonstrates possible avoidance of the undesirable effects in brain-injured patients [13, 14].

During general anesthesia, in patients without neurological disease, the cerebrovascular autoregulation seems to be maintained between 0.5 and 1.0 minimum alveolar concentration (MAC) of sevoflurane, although the autoregulation is slightly impaired with MAC above 1.0. However, some authors suggested that cerebral autoregulation is maintained even with higher MAC (1.2 and 1.5 MAC) [15]. Compared to sevoflurane, the use of halothane [16] is associated with lower vessel resistance and higher mean flow velocity during general anesthesia. The effect of isoflurane on cerebral FVs however is discordant [17,

18]. Many authors consider the use of isoflurane [24] on cerebral hemodynamics as safe; however, Nishiyama et al. [25] compared cerebrovascular carbon dioxide reactivity assessed through TCD during general anesthesia with sevoflurane and isoflurane in patients without known cerebral disease and found that FV was significantly lower in the isoflurane group at $PCO_2 = 20$–40 mm Hg than in the sevoflurane group. Moreover, they found that the rate of change in cerebral blood flow caused by variations of CO_2 tension was greater during the administration of isoflurane anesthesia compared with sevoflurane.

Holmström et al. [19] assessed the dose-dependent vasodilatory effects at hypocapnia of desflurane, sevoflurane, and isoflurane administered in a randomized order at 0.5 and 1.0 MAC in a pig experimental model. Cerebral and systemic variables were recorded at two different levels of CO_2 (normocapnia vs. hypocapnia). At 0.5 MAC, all the agents had similar effects on CBF at hypocapnia. However, the authors found a more pronounced cerebral vasodilation at hypocapnia with higher doses of desflurane than with sevoflurane or isoflurane, concluding that desflurane might be less suitable than other agents in neurosurgical procedures.

Among volatile agents, sevoflurane seems to have the least effect on middle cerebral artery blood flow velocities; however, it has shown to determinate a reduction in cerebrovascular carbon dioxide reactivity at and above CO_2 of 45 mm Hg at 1.0 and 1.5 MAC, which is even reduced with the addition of nitrous oxide [20].

The addition of nitrous oxide can also determinate significant increase in CBF and reduction in autoregulatory indices and needs to be avoided [21].

24.5.2 Intravenous Anesthetics

Intravenous anesthesia is considered the technique of choice for neurosurgical procedures since, compared to inhalation technique, is associated with less pronounced vasodilating effect on cerebral vessels [22].

However, investigations comparing the cerebral hemodynamic effects during inhalation or intravenous anesthesia are conflicting.

Recent findings confirm that the use of sevoflurane, compared to propofol sedation, can decrease more significantly MAP and CPP in neurocritical care population, with consequent ICP increases [23]. However, Marval et al. [24] found that estimated CPP (eCPP), calculated using an established formula, decreased significantly in the propofol group (median, from 58 to 41 mm Hg) but not in the sevoflurane group (from 60 to 62 mm Hg) in 23 healthy patients undergoing non-neurosurgical procedures monitored with TCD.

Finally, some authors demonstrated [25] that, in patients undergoing intracranial tumors resection, cerebral blood flow velocity was not significantly different between sevoflurane- and propofol-anesthetized patients at the comparable depth of anesthesia, suggesting a role of inhalation anesthesia in neurosurgical procedures.

Propofol is the intravenous anesthetic drug of choice and it is commonly used as a first-line therapy for sedation and control of intracranial pressure in head-injured patients. Compared to thiopental, the use of propofol during electroconvulsive therapy resulted in minor cerebral blood flow velocity changes [26].

Steiner et al. [27] examined the effect of increasing propofol plasmatic concentration on pressure autoregulation in head-injured patients. They administered norepinephrine to achieve CPP of 70 and 85 mm Hg at each different propofol concentration. The authors found that at high propofol concentration TCD-derived flow velocities were significantly lower than at the moderate concentration, but that autoregulation was impaired. In their study, Steiner et al. therefore demonstrated that the cerebrovascular effects of propofol in head-injured patients are different from those observed in healthy individuals, and large doses of propofol should be used cautiously in this group of patients.

Opioids are frequently used in patients with cerebral injury despite clinical reports suggest that these compounds may increase ICP. Some authors suggest that fentanyl and sufentanil can elevate ICP [28]. However, increases in ICP along with infusion of opioids are generally associated with decreases in MAP, and a rise in ICP is related to autoregulatory vasodilation and increased cerebral blood volume secondary to systemic hypotension.

Indeed, de Nadal et al. demonstrated that morphine and fentanyl transiently increase ICP in response to ABP decrease in patients with preserved and impaired cerebrovascular autoregulation but induced no significant variations in CBF estimated by TCD sonography. [29]

24.6 Transcranial Doppler Ultrasonography in Neurocritical Care Monitoring

TCD presents a wide range of clinical application in the neurointensive care settings (Table 24.2).

24.6.1 Non-invasive ICP and CPP Assessment

Monitoring and targeted management of ICP and CPP are widely advocated for patients with severe head injuries as intracranial hypertension is an important cause of morbidity and mortality [30]. Therefore, ICP and CPP evaluation is crucial in many neurological diseases such as traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), and stroke [31].

The gold standard for ICP measurement is invasive. However, invasive ICP monitoring is associated with a wide range of possible complications including infection and hemorrhage [32]; therefore, a noninvasive measurement of ICP can be invaluable in the management of many neurological patients [33]. TCD is one possible tool to assess noninvasive ICP (nICP) and CPP, as increased ICP produces specific changes in cerebral blood FV, with diastolic FV being particularly sensitive [10].

Gosling pulsatility index (gPI) is one of the first measures derived from the TCD waveform that has been studied to assess ICP (Fig. 24.7),

Table 24.2 Clinical applications of transcranial Doppler

Traumatic brain injury	Noninvasive ICP and CPP estimation
	Autoregulation
	Compliance and cerebrovascular dynamics
SAH (Aneurysms and AVM)	Vasospasm
	Autoregulation
Stroke	Diagnosis and treatment of ischemic stroke
Hydrocephalus	Infusion study and cerebral reserve and compliance
	Noninvasive ICP and CPP
Brain death	Diagnosis of brain death
Sickle cell disease	Risk from a spectrum of brain injuries that include subclinical infarction, acute stroke and hemorrhage; screening of children between 2- and 6-years old is recommended on a 6–12 monthly basis, involving measurement of the time-averaged mean FV in bilateral MCA, bifurcation, distal ICA, ACA, PCA, and BA
Right to left CARDIAC shunt	Evaluation of paradoxical embolism through right to left cardiopulmonary shunts (e.g., patent foramen ovale)
Central nervous system infections	Noninvasive ICP and cerebrovascular dynamic
Peri-procedural/operative	Autoregulation Noninvasive ICP and CPP
Liver failure and Hepatic encephalopathy	Noninvasive ICP estimation and prognosis for acute liver failure
Preeclampsia	Assessment of autoregulation and FV as prognostic for preeclampsia
Sepsis	Assessing cerebral perfusion changes in septic patients as risk of sepsis-associated encephalopathy

but reports on its usefulness for predicting ICP and CPP are discordant [6, 8].

Bellner [6] found a significant correlation ($R = 0.94$, $p < 0.0001$) between ICP and PI but other authors found weak correlation between PI and ICP [9]. Some other studies proposed methods based on the primarily intended calculation of non-invasive cerebral perfusion pressure (nCPP), and secondarily calculating noninvasive ICP based on the assumption that nICP = ABP – nCPP [42, 43].

Czosnyka et al. [34] proposed a similar but modified formula for estimation of CPP and demonstrated that the correlation between noninvasive CPP (nCPP) and measured CPP was 0.73 ($p < 10^{-6}$). The absolute difference between real CPP and nCPP was less than 10 mm Hg in 89% of measurements and less than 13 mm Hg in 92% of measurements.

Recently, Varsos et al. proposed a method to estimate CPP based on critical closing pressure (CrCP) which represents a threshold of ABP, below which the blood pressure in the brain vasculature is inadequate to prevent the collapse and

cessation of blood flow [35]. The authors found a good correlation between nCPP and measured CPP ($R = 0.85$, $p < 0.001$), with a mean (±SD) difference of 4.02 ± 6.01 mmHg. In 83.3% of the cases, the estimation error was below 10 mmHg.

In summary, there is a considerable variability in the results from studies assessing the accuracy of TCD in the detection of ICP and CPP. None of these methods seem to be accurate enough to be used as a replacement for invasive ICP measurement, but TCD can still be useful in many situations, including when the patient presents contraindication for the insertion or invasive ICP monitoring or when the indications for ICP are not met (Fig. 24.8).

24.6.2 Vasospasm and SAH

Aneurysmal subarachnoid hemorrhage (aSAH) occurs with an incidence of 6–10 per 100,000 cases per years [36] and represents an important cause of morbidity and mortality.
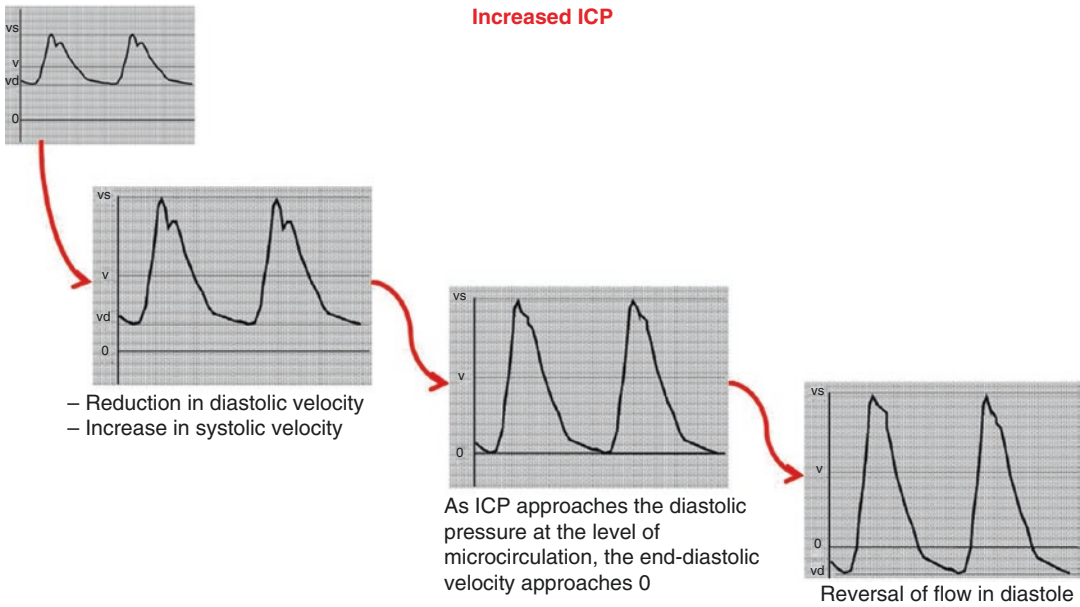
Increased ICP

– Reduction in diastolic velocity
– Increase in systolic velocity

As ICP approaches the diastolic pressure at the level of microcirculation, the end-diastolic velocity approaches 0

Reversal of flow in diastole

Fig. 24.8 How increased may affect cerebral blood flow velocities as demonstrated by TCCS

Table 24.3 Grading of vasospasm

Vasospasm of the MCA	FVm (cm/s)
Mild (<25% narrowing)	<120
Moderate (25–50% narrowing)	120–200
Severe (>50% narrowing)	>200

Abbreviations: MCA middle cerebral artery, *FVm* mean flow velocity

Vasospasm after aSAH is another important cause of mortality and morbidity. It usually occurs 3–14 days following aSAH, and it is known to be one of the causes leading to new ischemic neurological deficits [37]. Despite angiography still being the gold standard for the detection of vasospasm, TCD can be used for the assessment and detection of vasospasm after aSAH [38] as the constriction of the cerebral vessels leads to an increase of the cerebral blood flow velocities.

TCD has a good ability in the prediction of vasospasm. In particular, mean flow velocity >120 cm/s on the MCA was found to have a specificity of 72% and sensitivity of 88% for angiographic vasospasm (Table 24.3) [39].

The Lindegaard ratio (LR) is a TCD-derived index which is normally used to differentiate between the increase in FV related to systemic hyperdynamic flow and the increase secondary to vasospasm, by comparing intra-extra cranial blood flow velocities.

LR is calculated according to the following formula:

$$LR = \frac{MCA\,MFV}{\text{extracranial}\,ICA\,MFV}$$

When increased flow velocity is related to hyperemia, it affects both intracranial and extracranial portion of the ICA (LR < 3); when vasospasm is the cause of increased flow velocity, the extracranial portion of the ICA is unaffected and LR is >3 (Fig. 24.9). In the posterior circulation, a modified LI is generally used with a value >2 as threshold to indicate vasospasm [40]:

Modified LR = BA (FVm)/VA (FVm).

An approach to the interpretation of the flow velocities and the Lindegaard index in the context of vasospasm is presented in Fig. 24.10.

24.6.3 Autoregulation

Cerebral autoregulation is the intrinsic ability of the brain to maintain a stable CBF despite
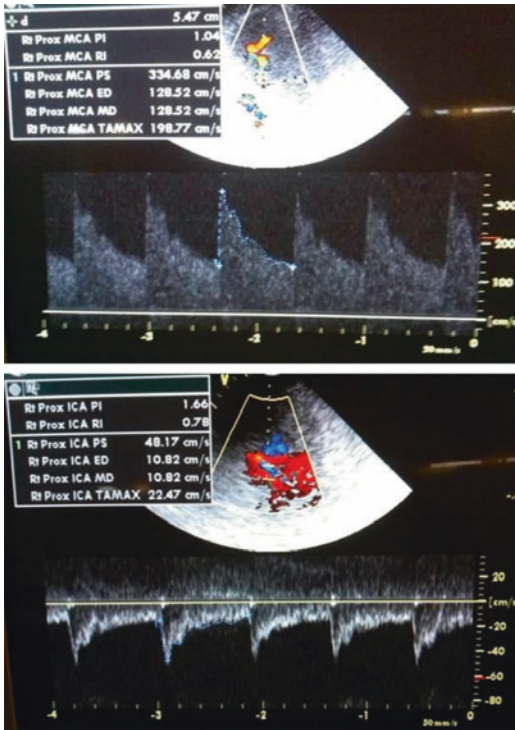
Lindegaard index

$$LI = \frac{FV_{MCA}}{FV_{ecICA}}$$

- The Lindegaard ration helps determine whether the increase in MCA velocity is due to vasospasm or due to hyper – dynamic flow

- $3.00 \leq LI \leq 5.99$: mild to moderate

- $LI \geq 6.00$: severe

Lindegaard index: 8:8 (198.77/22.47)

Fig. 24.9 Lindegaard index (*LI*) formula and example of severely elevated LI
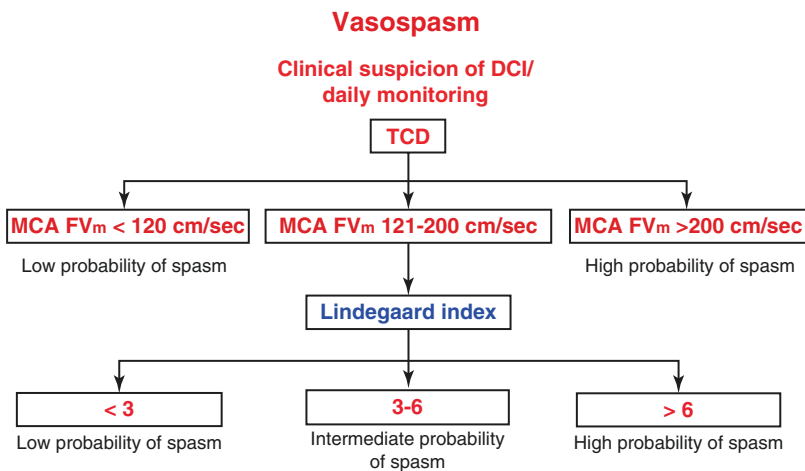

Fig. 24.10 Approach to the interpretation of the flow velocities and the Lindegaard index in the context of vasospasm

variations in cerebral perfusion pressure between certain limits of pressure (50–150 mmHg in normotensive patients) [41]. Impairment of autoregulation has been demonstrated in many neurocritical care conditions, and it is related to poor outcome.

Monitoring of cerebral autoregulation has been performed for decades under steady-state conditions in clinical practice. TCD has been applied as a static model to autoregulatory testing in patients using the static autoregulatory index (sARI) or static rate of regulation (sROR),

defined as the percentage of change in CVR with respect to the percentage of change in CPP [42].

However, static assessment of autoregulation is often too simplistic as it does not take in account a number of factors including the different upper and lower limits of autoregulation or different slopes of the "autoregulatory zone" among different individuals.

A recent approach used TCD for the investigation of dynamic cerebral autoregulation given its high temporal resolution, which allows to measure the timing of the changes of CBF to the CPP/(ABP) challenge [43].

TCD can allow the calculation of an index of autoregulation called mean flow index (Mx), which is calculated as the correlation coefficient between FVm and CPP; an Mx value of zero or negative indicates preserved autoregulation, whereas a positive correlation between ABP (or CPP) and CBF indicates impaired autoregulation.

The study of autoregulation through TCD has been applied in many clinical scenarios.

In patients with stroke, TCD has demonstrated to be able to detect an impairment in cerebral autoregulation of the pathologic hemisphere and showed an association of this impairment with poor outcome [44]. Moreover, impaired autoregulation assessed with Mx index has shown to be strongly associated with poor outcome at 6 months in patients after TBI [45].

Similarly to TBI, impaired cerebral autoregulation seems to play a significant role in the pathophysiology of vasospasm and delayed cerebral ischemia (DCI) after SAH. Budohoski et al. demonstrated that patients with worse autoregulation after SAH are more likely to develop delayed cerebral ischemia (DCI) independently to the incidence of vasospasm [46] and that impairment of autoregulation can be detected before vasospasm occurs.

Finally, in patients with ICA stenosis, impaired autoregulation assessed by Mx observed in the pathological stenotic or occlusive arteries has shown to be correlated with the degree of stenosis and is considered as a tool to identify patients at risk for need of surgical decompressive craniectomy [47].

24.6.4 Brain Death

Brain death is an irreversible cessation of the brain and brainstem functions. Its diagnosis implies several medical, ethical, and legal implications.

Currently, brain death is diagnosed by clinical neurological examination and confirmatory instrumental tests in some clinical cases, such as EEG, angiography with multi-slice computed tomography (CTA), brain scintigraphy or TCD, according to the legal requirements in each individual country.

The use of TCD in brain dead has been first described in 1974, and it is an alternative confirmatory test. It is able to demonstrate cerebral circulatory arrest associated to brain death, especially when neurological examination is not possible.

The conditions for establishing a diagnosis of cerebral circulatory arrest using TCD include the knowledge of the cause of coma, and the exclusion of factors that may alter the neurological findings, including hypothermia, metabolic alterations, and intoxications. Moreover, during the TCD measurements, the patient has to be hemodynamically stable with a blood pressure no lower than 90/50 mmHg, and $PaCO_2$ 35–45 mmHg.

Published criteria [48] for the diagnosis of cerebral circulatory arrest on TCD state that one of the following waveforms must be observed in the middle cerebral artery, basilar artery, and internal carotid artery bilaterally by two expert sonographers:

1. An oscillating waveform (equal systolic forward flow and diastolic reversed flow) (Fig. 24.11)
2. Small systolic spikes of < 200 ms duration and < 50 cm/s PSV with no diastolic flow (Fig. 24.12), or
3. Disappearance of intracranial flow

The examinations should be repeated twice at least 30 min apart.

Despite the large number of limitations in the use of TCD for the diagnosis of brain dead (operator-dependent technique, absence of acoustic window in 10–20% of patients, difficulty exploring posterior circulation in critically ill patients, false-negative results in patients with anoxia or with open skull), a meta-analysis
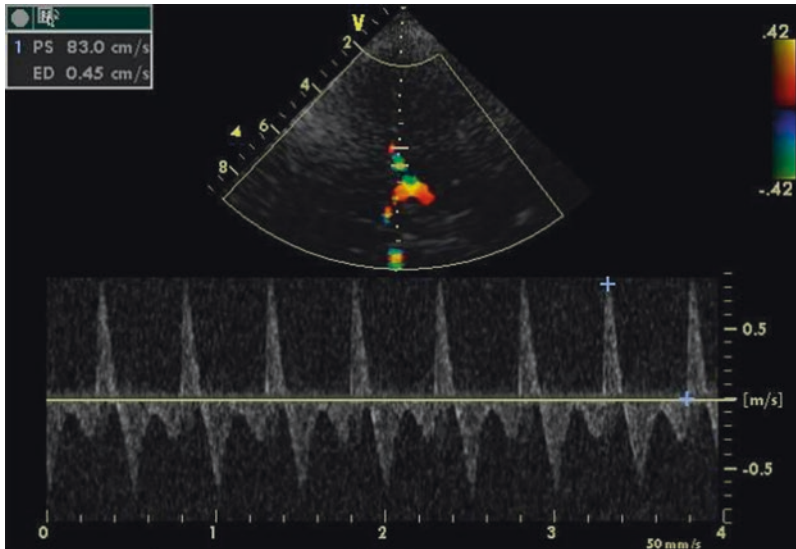
Fig. 24.11 Example of diastolic flow reversal in the context of malignant intracranial hypertension
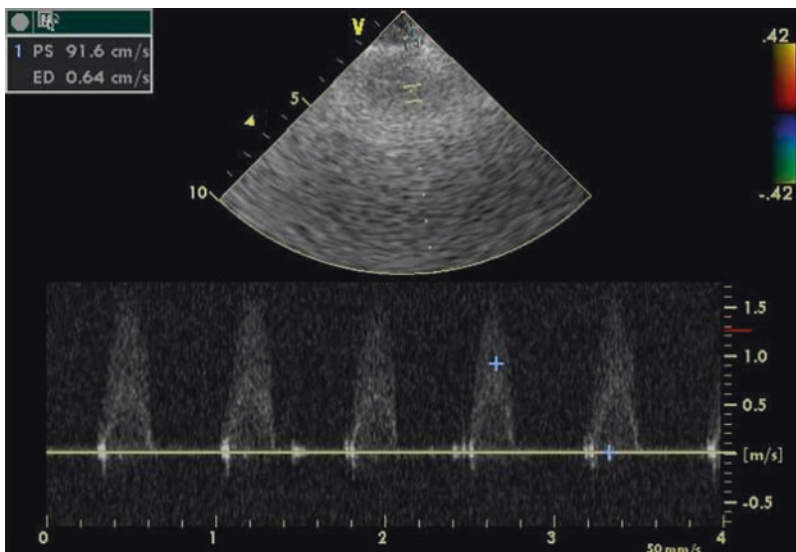

Fig. 24.12 Example of absence of diastolic flow in the context of malignant intracranial hypertension

published in 2006 [49] reported a sensitivity of 95% and a specificity of 99%.

24.7 Other Applications

TCD has been used for the diagnosis, prognosis, and treatment of ischemic stroke.

It has been demonstrated to be a reliable prognostic indicator in MCA occlusive stroke [50] and may also have a role in the prediction of out-come in these patients, according to the site and severity of occlusion observed.

Besides the common previously described applications in neurointensive care settings, TCD has been successfully applied even in the intraoperative settings, in order to assess nCPP and nICP in surgical procedures at risk to increase intracranial hypertension [5] such as laparoscopic procedures with pneumoperitoneum and Trendelenburg position, as well as for neuromonitoring during cardiac surgery or carotid endarterectomy . Finally, growing and

recent evidences support the use of TCD even in metabolic coma (such as during liver transplant or hepatic encephalopathy) or in pregnant patients, to assess autoregulation and cerebrovascular changes as prognostic factor for preeclampsia.

24.7.1 Limitations of TCD and TCCS

TCD presents several technical limitations. First, the two main assumptions and limitations that govern the use of TCD as an indirect measure of CBF are a constant vessel diameter and an unchanged angle of insonation during the measurements (despite TCCS allows correction of angle of insonation). As demonstrated by Clark et al. [51], MCA blood-flow velocity is a useful index of CBF response to changes in arterial PCO_2 during O_2 breathing at rest. However, FV evaluated by TCD is proportional to CBF only when vessel cross-sectional area remains constant. Thus, the results of any TCD study of CBF should always be interpreted with caution, keeping in mind the possibility that cerebral vessel diameter has changed. With every ultrasound exam, there is an operator-dependent variability, despite the intra-observer and inter-observer variability during TCD examinations has been reported to be good [52].

In a recent study on healthy volunteers and patients with aSAH, TCCS measurement variability resulted to be wider in patient measurements than in healthy volunteers (Bland-Altman limits of agreement 0.62–1.61 in patients and 0.67–1.50 in controls). This discrepancy can be explained by a higher degree of error in patients with angiographic vasospasm, where the caliber of the vessels is altered

Another limitation is that up to 20% of patients do not have a proper temporal window which prevents US transmission [52].

Moreover, since measurements are frequently only taken from the MCA, cerebrovascular changes in the posterior circulation may not be detected [44].

Finally, there are several anatomical variants and the direction and anatomy of the vessels can vary up to 52% of patients [53].

Conclusion

TCD is a noninvasive, safe, accessible technique for the bedside monitoring of static and dynamic cerebral flow and treatment response.

In neurointensive care settings, real-time monitoring of TCD-derived indices may provide important information regarding the onset of cerebrovascular alterations and facilitate clinical management of cerebral pathologies. Despite it presents several limitations, TCD remains an important tool for the assessment of cerebral hemodynamics in critically ill patients.

References

1. Aaslid R, Markwalder TM, Nornes H. Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. J Neurosurg [Internet]. 1982;57(6):769–74. Available from: <Go to ISI>://WOS:A1982PR90500007.
2. You Y, Hao Q, Leung T, Mok V, Chen X, Lau A, et al. Detection of the siphon internal carotid artery stenosis: transcranial Doppler versus digital subtraction angiography. J Neuroimaging. 2010;20:234–9.
3. Lowe LH, Bulas DI. Transcranial Doppler imaging in children: Sickle cell screening and beyond. Pediatr Radiol. 2005;35(1):54–65.
4. Naqvi J, Yap KH, Ahmad G, Ghosh J. Transcranial Doppler ultrasound: a review of the physical principles and major applications in critical care. Int J Vasc Med. 2013;2013:629378.
5. Cardim D, Robba C, Bohdanowicz M, Donnelly J, Cabella B, Liu X, et al. Non-invasive monitoring of intracranial pressure using transcranial Doppler ultrasonography: is it possible? Neurocrit Care. 2016;1–19
6. 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(1):45–51.
7. Robba C, Donnelly J, Bertuetti R, Cardim D, Sekhon MS, Aries M, et al. Doppler non-invasive monitoring of ICP in an animal model of acute intracranial hypertension. Neurocrit Care. 2015;23(3):419–26.
8. De Riva N, Budohoski KP, Smielewski P, Kasprowicz M, Zweifel C, Steiner LA, et al. Transcranial doppler pulsatility index: what it is and what it isn't. Neurocrit Care. 2012;17(1):58–66.
9. Giller CA, Hodges K, Batjer HH. Transcranial Doppler pulsatility in vasodilation and stenosis. J Neurosurg. 1990;72:901–6.
10. Czosnyka M, Richards HK, Whitehouse HE, Pickard JD. Relationship between transcranial Doppler-determined pulsatility index and cerebrovascular resistance: an experimental study. J Neurosurg. 1996;84(1):79–84.
11. Bundgaard H, von Oettingen G, Larsen KM, Landsfeldt U, Jensen KA, Nielsen E, et al. Effects of sevoflurane on intracranial pressure, cerebral blood flow and cerebral metabolism. A dose-response study in patients subjected to craniotomy for cerebral tumours. Acta Anaesthesiol Scand. 1998;42(6):621–7.

12. Matta BF, Heath KJ, Tipping K, Summors AC. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. Anesthesiology. 1999;91(3):677–80.

13. Kaisti KK, Långsjö JW, Aalto S, Oikonen V, Sipilä H, Teräs M, et al. Effects of sevoflurane, propofol, and adjunct nitrous oxide on regional cerebral blood flow, oxygen consumption, and blood volume in humans. Anesthesiology [Internet]. 2003;99(3):603–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12960544.

14. Kaisti KK, Metsahonkala L, Teras M, Oikonen V, Aalto S, Jaaskelainen S, et al. Effects of surgical levels of propofol and sevoflurane anesthesia on cerebral blood flow in healthy subjects studied with positron emission tomography. Anesthesiology [Internet]. 2002;96(6):1358–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12170048.

15. Ogawa Y, Iwasaki KI, Shibata S, Kato J, Ogawa S, Oi Y. The effect of sevoflurane on dynamic cerebral blood flow autoregulation assessed by spectral and transfer function analysis. Anesth Analg. 2006;102(2):552–9.

16. Monkhoff M, Schwarz U, Gerber A, Fanconi S, Banziger O. The effects of sevoflurane and halothane anesthesia on cerebral blood flow velocity in children [Internet]. Anesth Analg. 2001;92(4):891–6. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11273920.

17. Brosnan RJ, Steffey EP, LeCouteur RA, Esteller-Vico A, Vaughan B, Liu IKM. Effects of isoflurane anesthesia on cerebrovascular autoregulation in horses. Am J Vet Res. 2011;72(1):18–24.

18. Nishiyama T, Matsukawa T, Yokoyama T, Hanaoka K. Cerebrovascular carbon dioxide reactivity during general anesthesia: a comparison between sevoflurane and isoflurane. Anesth Analg [Internet]. 1999;89(6):1437–41. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10589623.

19. Holmström A, Rosén I, Åkeson J. Desflurane results in higher cerebral blood flow than sevoflurane or isoflurane at hypocapnia in pigs. Acta Anaesthesiol Scand. 2004;48(4):400–4.

20. Wilson-Smith E, Karsli C, Luginbuehl I, Bissonnette B. Effect of nitrous oxide on cerebrovascular reactivity to carbon dioxide in children during sevoflurane anaesthesia. Br J Anaesth. 2003;91(2):190–5.

21. Iacopino DG, Conti A, Battaglia C, Siliotti C, Lucanto T, Santamaria LB, et al. Transcranial Doppler ultrasound study of the effects of nitrous oxide on cerebral autoregulation during neurosurgical anesthesia: a randomized controlled trial. J Neurosurg [Internet]. 2003;99(1):58–64. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12854745.

22. Villa F, Iacca C, Molinari AF, Giussani C, Aletti G, Pesenti A, et al. Inhalation versus endovenous sedation in subarachnoid hemorrhage patients: effects on regional cerebral blood flow. Crit Care Med [Internet]. 2012;40(10):2797–804. . Available from: http://www.ncbi.nlm.nih.gov/pubmed/22824929.

23. Purrucker JC, Renzland J, Uhlmann L, Bruckner T, Hacke W, Steiner T, et al. Volatile sedation with sevoflurane in intensive care patients with acute stroke or subarachnoid haemorrhage using AnaConDa(R): an observational study. Br J Anaesth [Internet]. 2015;114(March):934–43. Available from: http://bja.oxfordjournals.org/lookup/doi/10.1093/bja/aev070.

24. Marval PD, Perrin ME, Hancock SM, Mahajan RP. The effects of propofol or sevoflurane on the estimated cerebral perfusion pressure and zero flow pressure. Anesth Analg. 2005;100(3):835–40.

25. Banevičius G, Rugytė D, Macas A, Tamašauskas A, Stankevičius E. The effects of sevoflurane and propofol on cerebral hemodynamics during intracranial tumors surgery under monitoring the depth of anesthesia. Medicina (Kaunas) [Internet]. 2010;46(11):743–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21467832.

26. Saito S, Kadoi Y, Nara T, Sudo M, Obata H, Morita T, et al. The comparative effects of propofol versus thiopental on middle cerebral artery blood flow velocity during electroconvulsive therapy [Internet]. Anesth Analg. 2000;91(6):1531–6. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11094013.

27. Steiner LA, Johnston AJ, Chatfield DA, Czosnyka M, Coleman MR, Coles JP, et al. The effects of large-dose propofol on cerebrovascular pressure autoregulation in head-injured patients. Anesth Analg. 2003;97:572–6. table of contents

28. Albanese J, Durbec O, Viviand X, Potie F, Alliez B, Martin C. Sufentanil increases intracranial pressure in patients with head trauma. Anesthesiology. 1993;79(3):493–7.

29. de Nadal M, Munar F, Poca MA, Sahuquillo J, Garnacho A, Rosselló J. Cerebral hemodynamic effects of morphine and fentanyl in patients with severe head injury: absence of correlation to cerebral autoregulation. Anesthesiology. 2000;92(1):11–9.

30. Marmarou A, Anderson RL, Ward JD, Choi SC, Young HF, Eisenberg HM, et al. Impact of ICP instability and hypotension on outcome in patients with severe head trauma. J Neurosurg. 1991;75(Supplement):S59–66.

31. Miller JD, Becker DP, Ward JD. Significance of intracranial hypertension in severe head injury. J Neurosurg [Internet]. 1977;47(4):503. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L8193896\nhttp://sfx.library.uu.nl/utrecht?sid=EMBASE&issn=00223085&id=doi:&atitle=Significance+of+intracranial+hypertension+in+severe+head+injury&stitle=J.+NEUROSURG.&title=Journal+.

32. Holloway KL, Barnes T, Choi S, Bullock R, Marshall LF, Eisenberg HM, et al. Ventriculostomy infections: the effect of monitoring duration and catheter exchange in 584 patients. J Neurosurg. 1996;85(3):419–24.

33. Robba C, Bacigaluppi S, Cardim D, Donnelly J, Bertuccio A, Czosnyka M. Non-invasive assessment of intracranial pressure. Acta Neurologica Scand. 2016;134(1):4–21.

34. 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(5):802–8.

35. Varsos GV, Kolias AG, Smielewski P, Brady KM, Varsos VG, Hutchinson PJ, et al. A noninvasive estimation of cerebral perfusion pressure using critical closing pressure. J Neurosurg. 2015;123(3):638–48.

36. Rincon F, Rossenwasser RH, Dumont A. The epidemiology of admissions of nontraumatic subarachnoid hemorrhage in the United States. Neurosurgery. 2013;73(2):217–22.

37. Diringer MN, Bleck TP, Claude Hemphill J, Menon D, Shutter L, Vespa P, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. Neurocrit Care [Internet]. 2011; [cited 2014 Nov 25];15(2):211–40. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21773873.

38. Kistka H, Dewan MC, Mocco J. Evidence-based cerebral vasospasm surveillance. Neurol Res Int [Internet]. 2013;2013:256713. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3686086&tool=pmcentrez&rendertype=abstract.

39. 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(2):291–303.

40. Soustiel JF, Shik V, Feinsod M. Basilar vasospasm following spontaneous and traumatic subarachnoid haemorrhage: clinical implications. Acta Neurochir 2002;144 (2):137–44.

41. Czosnyka M, Smielewski P, Piechnik S, Pickard JD. Clinical significance of cerebral autoregulation. Acta Neurochir Suppl [Internet]. 2002;81:117–9. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12168280.

42. Panerai RB. Transcranial Doppler for evaluation of cerebral autoregulation. Clin Auton Res [Internet]. 2009 [cited 2014 Nov 18];19(4):197–211. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19370374.

43. Donnelly J, Aries MJ, Czosnyka M. Further understanding of cerebral autoregulation at the bedside: possible implications for future therapy. Expert Rev Neurother [Internet]. 2015;15(2):169–85. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25614952.

44. Aries MJH, Elting JW, De Keyser J, Kremer BPH, Vroomen PCAJ. Cerebral autoregulation in stroke: a review of transcranial doppler studies. Stroke. 2010;41(11):2697–704.

45. Czosnyka M, Smielewski P, Kirkpatrick P, Menon DK, Pickard JD. Monitoring of cerebral autoregulation in head-injured patients. Stroke [Internet]. 1996;27(10):1829–34. Available from: http://acs.hcn.com.au?acc=36422&url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med4&AN=8841340.

46. Budohoski KP, Czosnyka M, Smielewski P, Kasprowicz M, Helmy A, Bulters D, et al. Impairment of cerebral autoregulation predicts delayed cerebral ischemia after subarachnoid hemorrhage: a prospective observational study. Stroke [Internet]. 2012; [cited 2014 Jun 16];43(12):3230–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23150652.

47. 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(9):2138–44.

48. Powers AD, Graeber MC, Smith RR. Transcranial Doppler ultrasonography in the determination of brain death. Neurosurgery. 1989;24(6):884–9.

49. Monteiro LM, Bollen CW, Van Huffelen AC, Ackerstaff RGA, Jansen NJG, Van Vught AJ. Transcranial Doppler ultrasonography to confirm brain death: a meta-analysis. Intensive Care Med. 2006;32(12):1937–44.

50. 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(24):2897–902.

51. 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.

52. Bazan R, Braga GP, Luvizutto GJ, Hueb JC, Hokama NK, Zanati Bazan SG, et al. Evaluation of the temporal acoustic window for transcranial Doppler in a multi-ethnic population in Brazil. Ultrasound Med Biol. 2015;41(8):2131–4.

53. Iqbal S. A comprehensive study of the anatomical variations of the circle of Willis in adult human brains. J Clin Diagn Res. 2013;7(11):2423–7.