Doppler Haemodynamics of Cerebral Venous Return

Erica Menegatti and Paolo Zamboni*

Vascular Diseases Center, University of Ferrara, Italy

Abstract: Physiologic functioning of the cerebrovenous system is indispensable for maintaining normal brain function. However, in contrast to the cerebroarterial system, the cerebral venous return is not routinely investigated. Combined high-resolution echo-colour-Doppler (ECD) and transcranial colour coded Doppler sonography (TCCS) represents an ideal method to investigate the haemodynamics of cerebral venous return. TCCS-ECD is noninvasive, repeatable, cost-effective and permits to investigate the cerebral venous outflow in its dependence upon changes in posture and the alternating pressure gradients of the thoracic pump. Several authors reported normal parameters concerning related aspects of cerebral venous return. However, there is no ECD-TCCS standardization of what can be considered a normal venous return. The authors have summarized the current knowledge of the Doppler haemodynamics of the cerebrovenous system and propose a list of reproducible clinical parameters for its sonographic evaluation. In future, the development of this diagnostic technique could be of singular interest in iron-related inflammatory and neurodegenerative disorders like multiple sclerosis.

INTRODUCTION

Posture and respiratory movements play a fundamental role in ensuring the correct cerebrospinal venous outflow. At the time of expiration, intrathoracic pressure is approximately -5 cm H₂O and forced inspiration generates even lower intrathoracic pressures of about -8 cm H₂O (Schaller, 2004; Zamboni et al., 2007). The pressure gradients favour venous return to the right heart, which fact can be easily assessed with high-resolution ECD and TCCS, which thus constitute an ideal method for investigating the haemodynamics of cerebral venous return (Schaller, 2004; Valdueza et al., 2000; Gisolf et al., 2004; Schreiber et al., 2003; Doepp et al., 2004).

In addition, ECD showed a postural control of the extracranial outflow pathways, as follows: (Valdueza et al., 2000) the IJV is the predominant venous pathway in the supine position, as confirmed by an increased blood flow in that posture; redirection of venous flow to the VVs occurs in the upright position, with concomitant reduction of blood flow in the IJVs.

To the contrary, MR and selective injection venography are limited to evaluating cerebral venous haemodynamics under different postural and respiratory circumstances. Thereby, especially the latter provides excellent morphological but though exclusively static findings.

Several authors reported normal parameters after investigating different aspects of cerebral venous Doppler haemodynamics in the last decade. However, there is no ECD-TCCS standardisation of what can be considered a normal venous return. The authors have summarized the current knowledge of the Doppler haemodynamics of the cerebrovenous system and propose a list of parameters and a clinical methodology for reproducibly assessing them, that allow to tell whether cerebral venous outflow runs normally, or not.

ECD-TCCS EQUIPMENT AND PATIENT POSITION DURING THE INVESTIGATION

Nowadays the investigation of the cerebral venous haemodynamics can envisage the contemporaneous analysis of both the intracranial and extracranial pathways, by combining with the same ultrasound machine respectively the examination of the DCVs and main dural sinuses, by means of the TCCS probe (Baumgartner et al., 1997; Stoltz et al., 1999; Zamboni et al., 2007), with that of the IJVs-VVs by means of the ECD probe (Schaller, 2004; Valdueza et al., 2000; Gisolf et al., 2004; Schreiber et al., 2003; Doepp et al., 2004). The transducer used at the intracranial level is at low frequency, usually 2.5 MHz, whereas at the cervical level it is at high frequency, 7.5-10 MHz or more, according to the different depth of the veins respective to the body surface where the transducer is placed.

The posture of the subject under examination obtains, as indicated above, a crucial part determining the main route of cerebral outflow. For this reason the subject should be investigated at least in both supine and sitting position (0° and 90°), but it has further been proposed to assess venous flow from the brain with the body positioned at 0°, +15°, +30°, +45°, +90° in both the IJVs and VVs. (Valdueza et al., 2000). This objective can be realized with the subjects being positioned on a tilt bed.

TCCS VENOUS INVESTIGATION

The main parameters of the TCCS investigation of the intracranial veins are the diameter of the third ventricle (III V), and flow parameters which include direction, velocity and resistance index.
Assessment of Third Ventricle Diameter

According to the Monro-Kellie law, the sum of brain volume plus cerebro-spinal fluid (CSF), plus cerebral blood volume (CBV) always remains constant (Schaller, 2004). Therefore, an increase in venous pressure/volume determines a volume compensation achieved by changes in both extra- and intracellular cerebral fluid volume (Carmelo et al., 2002; Wey and Kontos, 1982). From this point of view, the assessment of the diameter of the III V is an important parameter, easy and rapid to assess by B-mode TCCS, for its being, interestingly, related to both CBV and CSF volume. In addition, III V measured by B-mode TCCS closely and significantly correlates with MRI assessment (Kallmann et al., 2004).

The transducer is placed at the level of the trans-temporal bone window, and the depth of the insonation is adjusted to 10 cm. At an insonation depth of about 7 cm it is possible to consistently identify the echo-lucent III V, limited by two echogenic bright margins, as well as the two comma-shaped frontal horns of the lateral ventricles (Kallmann et al., 2004; Zamboni et al., 2007). In normal subjects III V diameter is about 4 mm in the supine position (Kallmann et al., 2004), (Fig. 1).

Interestingly in multiple sclerosis it is significantly wider, and an increased diameter corresponds to an increased disability score. This finding is of course related to the tissue loss and a compliant reduced brain volume (Kallmann et al., 2004). However, it suggests, according to the Monro-Kellie hypothesis, also a relationship with modifications of CBV, which was found in multiple sclerosis (Wuerfel et al., 2004; Rashid et al., 2004).

Intracranial Venous Flow Direction

Physiological intracranial venous flow is mono-directional, and characterized by low velocity and low resistance index. It can be recorded again through the trans-temporal approach, but the trans-occipital or the trans-ophthalmic windows can be used as well (Baumgartner et al., 1997; Stoltz et al., 1999; Zamboni et al., 2007; Zipper and Stoltz, 2002; Valdueza et al., 1996). Subjects can be examined in both sitting and supine positions and the venous flow is enhanced by inviting the subject to breathe (Zamboni et al., 2007). Using the trans-temporal acoustic bone window, it is highly probable to insonate at least one of the DCVs, including basal veins of Rosenthal, great vein of Galen, and internal cerebral veins, according to criteria previously described (Valdueza et al., 1996; Stoltz et al., 1999; Zipper et al., 2002).

In a study, patients affected by multiple sclerosis were examined in both sitting and supine positions, demonstrating reflux flow. The reflux in the intracranial veins is defined as a flow recorded in a direction opposite to the physiologic one for a duration > 0.5 sec., a finding significantly different from the mono-directionality registered on normal volunteers.

In about 50% of multiple sclerosis patients TCCS demonstrated pathological venous reflux within DCVs and transverse sinuses during the activity of the thoracic pump. Such reflexes were absent in the DCVs in healthy subjects and while only 7% of healthy individuals exhibited venous reflexes in the transverse sinus (Zamboni et al., 2007).

EXTRACRANIAL DOPPLER VENOUS INVESTIGATION

Examination is performed with high frequency transducers as above reported. Subjects should be examined at least in sitting and supine positions, or better on a tilting bed with the body positioned at 0°, +15°, +30°, +45°, +90° (Valdueza et al., 2000). Either the IJVs and the VVs can be examined by using both the transversal and/or the longitudinal cervical access. The operator uses minimal pressure over the skin in order to prevent compressing the vein and thereby affecting the measurement, as previously reported (San Millan Ruiz et al., 2002; Valdueza et al., 2000; Gisolf et al., 2004; Schreiber et al., 2003; Doepp et al., 2004).

The operator can assess the following: flow direction, flow velocity, competence of the IJV valve, cross sectional area in relation to change in posture, duplex derived flowmetry, and anomalous morphology.
Assessment of Flow Direction and Doppler Flow Parameters

The flow direction, in either the IJVs or the VVs, can be measured during inspiration and/or expiration, but it is recommended to measure it in the respiratory pause (Valdueza et al., 2000); flow direction can be measured also with Valsalva for testing the competence of the jugular valve but this will be treated separately. The direction of flow can be analyzed either with the pulsed wave sample placed in the vessel, at a 60° angle, or with the Colour Coded Mode, by comparing the colour of the flow in the IJVs/VVs with that of the satellite carotid and/or vertebral artery, respectively (Fig. 2A, B).

According to consensus statements on peripheral vein ECD investigations, we define as monodirectional a flow always directed toward the heart. Flow is considered bidirectional when, in at least one of such conditions, we detect a flow reversal from its physiological direction for a duration < 0.5 sec. When the phase of reverse flow is > 0.5 sec, it is defined as venous reflux (Nicolaides et al., 2000; Coleridge-Smith et al., 2006).

Assessment of Doppler flowmetry in ml/min by using the softwares included in the package of the ultrasound equipment, is performed at the level of the thyroid gland for the IJVs and at the level of C5-C6 for VVs (Valdueza et al., 2000). Therefore, it has been suggested to record flow measurement beginning two minutes after the change in posture and after several deep breaths in order to permit blood redistribution in the venous system.

It is well apparent in Table 2 that predominance of the IJV in cerebrovenous drainage is limited to the supine position. In the erect position, the vertebral venous system represents the major outflow pathway. Moreover, in the supine position, a duplex derived-flowmetry of 700±270 ml/m was measured in normal volunteers. This was found to change completely, however, when the subject changed to the upright position, as the IJV flow fell to 70±100 ml/m, whereas in the VV it rose from 40±20 to 210±120 ml/m (Valdueza et al., 2000).

The apparent unexplained rest of about 450 ml/min in the standing posture represents the gravitational effect of the hydrostatic pressure, which causes the displacement of 70% of the total volume of blood below the heart level (Folkow and Neil, 1973).

From this point of view, the higher hydrostatic column in the valveless vertebral-azygos system in the erect position favours venous drainage through this route, rather than through the IJV.

Competence of the Jugular Valve

Although the presence of valves in the distal portion of the IJVs has been widely described by anatomists and pathologists, they can be even absent. IJV’s valves were found in 93% of the post-mortem studies, and in 87% of patients by
means of high resolution B-mode ultrasounds; the majority of unilateral valve were found on the right side (Lepori et al., 1998). 

As far as the competence of the venous valve is concerned, it is well established in Doppler haemodynamics to test it by means of the Valsalva manoeuvre. According to a recent study on reflux time cut-off values, we can consider reflux a flow reversal from its physiological direction for a duration > 0.88 sec across the IJVs valve (Nedelmann et al., 2005). It has been reported that 33% of healthy individuals showed unilateral or bilateral IJVs valve incompetence. However, reflux recorded in accordance to this condition of measurement is strongly associated with transient global amnesia, in 68% of cases, with significantly higher prevalence as compared to controls (Sander and Sander, 2005; Schreiber et al., 2005).

**B-Mode Detection of Anomalous IJVs Morphology**

It has been reported that it is possible to observe IJVs stenosis and, in contrast, also IJVs aneurysms. An asymmetry, defined as a cross sectional area (CSA) at least twice that of the contralateral IJV was noted in 62.5% of cases. In addition, stenosis of the IJVs with a CSA of 0.4 cm² or less was measured in 23% of cases (Lichtenstein et al., 2001).

To the contrary, in Sardinia frequently, IJVs aneurysms in the absence of trauma, AV fistula and thoracic malformation have been described.

The abnormal dilatation was related to a fibrotic wall with absence or reduction of smooth muscle cells suggesting a congenital/developmental malformation (Zamboni et al., 1990).

**Flow not Doppler Detectable in the IJVs and/or VVs**

It has been described that there occurs the absence of a Doppler detectable venous flow in the IJVs and/or VVs despite numerous deep inspirations. In normal subjects this finding was never observed with the head in any position but the supine, in 6 % of cases (Doepp et al., 2004).

**CSA Variation According to the Predominant Pathway of Cerebral Venous Drainage**

Δ CSA in the IJVs, obtained by subtracting the CSA measured in the supine from that in the sitting position, is a positive value in normal subjects, as clearly shown in Table 1 (Schaller, 2004; Valdueza et al., 2000; Gisolf et al., 2004; Schreiber et al., 2003).

In Fig. (3) the change in CSA in response to the change in posture, and the corresponding ΔCSA, are apparent: CSA is wider in the supine position and reduced in the sitting. It can be considered a pressure/volume relationship, in practice a

![Fig. (3).](image-url)
non-invasive compliance curve of the jugular system. In fact, CSA variation reflects the variation of blood volume which flows in the IJV (Table 1) in response to changes in hydrostatic pressure determined by the different bodily positions (Zamboni et al., 1997; Zamboni et al., 1998).

CONCLUSIONS AND PERSPECTIVES

The adequate functioning of the cerebrovenous system may be one of the most important factors indispensable for the maintenance of a normal brain function (Schaller, 2004). Still, in contrast to the cerebroarterial system, the cerebral venous return is not routinely investigated. This review marks the combination of ECD and TCCS as the ideal method for tracing individual variations and anomalies in the haemodynamics of cerebral venous return.

As yet TCCS-ECD has only been taken advantage of in the assessment of transient global amnesia and in multiple sclerosis, but this imaging technique might as well be used for elucidating further clinical conditions.

In multiple sclerosis, TCCS-ECD recommends itself for monitoring the progression of the disease through a faster and cheaper assessment of the diameter of the III V as compared to MRI. In perspective, it seems also promising to study the topographic relationship between the cerebral veins exhibiting reflux at TCCS together with the location of plaques found at MRI; particularly, MR susceptibility weighted imaging, which allows contemporaneous imaging of veins and plaques, offers even greater promise (Koopmans et al., 2008). Finally, in view of the increased iron deposits forming a constant feature of either chronic venous disorders or multiple sclerosis (Zamboni, 2006; Zivadinov and Bakshi, 2004), it should be interesting to measure, by means of MR susceptibility weighted imaging (Haacke et al., 2007), the amount of iron in plaques of multiple sclerosis, evaluating the plaques’ topographic correspondence with the refluxing cerebral veins.

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GLOSSARY AND ABBREVIATIONS

<table>
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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>ECD</td>
<td>EchoColor-Doppler</td>
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<td>TCCS</td>
<td>Transcranial color-coded Doppler sonography</td>
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<td>IJV</td>
<td>Internal Jugular Vein</td>
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<td>VV</td>
<td>Vertebral Vein</td>
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<td>DCVs</td>
<td>Deep cerebral veins, including internal cerebral vein, basal vein, Galen vein</td>
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<td>CSA</td>
<td>Cross sectional area of the IJV</td>
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<td>ΔCSA</td>
<td>Difference in CSA assessed in supine and sitting posture in the IJV</td>
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Basic requirement of venous haemodynamics = To permit, by a mono-directional flow, a drainage of a volume of blood per unit of time adequate to a certain territory. This assumption has to be valid in all conditions.

Reflux = Venous flow reversal to the physiologic direction for a duration > 0.88 sec in the extracranial pathways, and > 0.50 sec in the DCVs.

REFERENCES


