CEREBRAL VENOUS CIRCULATORY SYSTEM EVALUATION BY ULTRASONOGRAPHY

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SUMMARY – Venous system can be classified as pulmonary veins, systemic veins and venous sinuses that are present only within the skull. Cerebral venous system is divided into two main parts, the superficial and the deep system. The main assignment of veins is to carry away deoxygenated blood and other maleficient materials from the tissues towards the heart. Veins have thinner walls and larger lumina than arteries. Between 60% and 70% of the total blood volume is found in veins. The major factors that influence venous function are the respiratory cycle, venous tone, the function of the right heart, gravity, and the muscle pump. Venous system, in general, can be presented by selective venography, Doppler sonography, computed tomography (CT) venography and magnetic resonance (MR) venography, and cerebral venous system can be displayed by selective venography, cerebral CT venography, cerebral MR venography, and specialized extracranial and transcranial Doppler sonography. The aim of this paper is to show the possibilities of intracranial and extracranial ultrasound evaluation of the head and neck venous circulation and chronic cerebrospinal venous insufficiency as one of the most common pathologies evaluated as part of neurodegenerative processes in the central nervous system.

Key words: *Veins – radiography; Veins – ultrasonography; Cerebral veins – ultrasonography; Cerebrovascular disorders; Chronic cerebrospinal venous insufficiency; Transcranial doppler sonography; Zamboni protocol*

Introduction

The main components of the human cardiovascular system are heart, blood and blood vessels. Blood vessel system consists of a large network of arteries, arterioles, capillaries, venules and veins. The main assignment of arteries is to deliver oxygen and nutrients to all parts of the body, while the main assignment of veins is to remove carbon dioxide and maleficent materials from cells and tissues in order to maintain body homeostasis. Neurodegenerative disorders are usually connected with insufficient arterial circulation, but in the underlying physiopathology venous circulation should also be evaluated. Nowadays, ultrasound is a well established tool in the evaluation of the arterial part of cerebral circulation, while venous circulation and its role in brain metabolism has been forgotten. In the last few years, the term chronic cerebrospinal venous insufficiency (CCSVI) has been used for disturbances of the morphology and flow in the head and neck venous circulation. This term is mostly used in new theories on the pathophysiology of multiple sclerosis and other neurodegenerative disorders. Therefore, radiologic as well as ultrasound criteria for CCSVI have been established.

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Human Circulatory System

Arterioles extend and branch out from an artery and lead to capillaries. Capillaries as the smallest of a body's blood vessels enable the exchange of water, oxygen, carbon dioxide and other nutrients and maleficent chemical substances between blood and surrounding tissues. Venules are blood vessels that drain blood directly from the capillary beds and unite to form a vein. The main assignment of veins is to carry away deoxygenated blood and other maleficent materials from the tissues towards the heart except for the pulmonary venous system that brings oxygenated blood from the pulmonary circulation back to the left atrium of the heart. Although most veins take blood back to the heart, there is also an exception. Portal veins carry blood between capillary beds.

Venous System Classification

Venous system can be classified as pulmonary veins, systemic veins and venous sinuses that are present only within the skull. Systemic veins whose course is close to the surface of the skin and have no corresponding arteries are superficial (cutaneous) veins. They channel blood from cutaneous tissues to deep veins *via* perforations in the deep fascia. Systemic veins situated deeper in the body and having corresponding arteries are deep veins. Most of the deep veins share routes with the arteries, and many of them are enclosed in the same sheaths. The precise location of veins is much more variable from person to person than that of arteries[1,2].

Venous System Morphology

Veins have thinner walls and larger lumina than arteries. Their walls consist of three layers. The outermost layer, called tunica externa or tunica adventitia, is at the same time the thickest layer on these vessels. It is composed of networks of elastic and collagen fibers, i.e. the connective tissue. Middle-layer, called tunica media, consists of bands of smooth muscle which are, in general, thin, as veins do not function primarily in a contractile manner. Comparing veins to arteries, veins possess a thinner tunica media, with little smooth muscle and elastic fibers, and are therefore more distensible. The interior of the venous wall is lined with endothelial cells that constitute the third layer called tunica intima. Some veins have valves that prevent the reflux of blood and aid in the return of blood against gravity. These valves are formed by folds of the innermost layer of the vein, tunica interna, into the lumen[1]. Because of their thin walls and larger lumina, veins act as low-resistance blood reservoirs. Between 60% and 70% of the total blood volume is found in veins. Consequently, veins are also called "capacitance vessels"[2].

Cerebral venous system morphology

Cerebral venous system can be divided into two basic components, a superficial and a deep system[3-5]. The superficial system comprises of sagittal sinuses and cortical veins and these drain superficial surfaces of both cerebral hemispheres. The superficial cerebral veins can be divided into three collecting systems, the first draining into the superior sagittal sinus and straight sinus, the second draining into the lateral sinus, and the third draining into the cavernous sinus. The superior sagittal sinus and straight sinus drain a major part of the cerebral hemispheres. The lateral sinuses receive blood from the cerebellum, the brain stem and posterior parts of the hemisphere. The cavernous sinuses drain blood from the orbits, the inferior parts of the frontal and parietal lobe, and from the superior and inferior petrosal sinuses. Blood from them flows into the internal jugular veins (IJV)[6].

The deep system comprises of lateral sinus, straight sinus and sigmoid sinus along with draining deeper cortical veins. In summary, blood from the deep white matter of the cerebral hemisphere and from the basal ganglia is drained by internal cerebral veins and basal veins of Rosenthal, which join to form the great vein of Galen that drains into the straight sinus[7].

Both systems, deep and superficial, mostly drain themselves into the IJVs. The cerebral veins and sinuses neither have valves nor tunica muscularis. Because they lack valves, blood flow is possible in different directions. Moreover, the cortical veins are linked by numerous anastamoses, allowing for the development of a collateral circulation. The lack of tunica muscularis permits veins to remain dilated. Venous sinuses are located between two rigid layers of dura mater[8]. This prevents their compression when intracranial pressure rises. The dural sinuses, especially the superior sagittal sinus, contain most of the arachnoid villi and granulations, in which absorption of the cerebrospinal fluid takes place[9].

Venous System Physiology

Venous return (VR) is the volume of blood that reaches the right heart. Many factors and variables affect VR. If these variables are kept constant, however, VR is inversely proportional to the central venous pressure. Also, in hemodynamically stable conditions, VR is roughly equal to cardiac output. The major factors that influence VR are the respiratory cycle, venous tone, the function of the right heart, gravity, and the muscle pump[10].

During the respiratory cycle, due to the negative intrathoracic pressure during inspiration, central venous pressure decreases, thereby increasing VR. Negative intrathoracic pressure is transmitted to the great thoracic veins, and as the diaphragm moves downward, the intra-abdominal pressure increases, thereby helping move blood toward the heart. When intrathoracic pressure increases, these mechanisms are reversed.

Venous tone affects VR by modifying the capacitance of veins and is primarily regulated by the autonomic system.

From the right ventricle, the blood is pumped out into the pulmonary circulation. When the ventricle contracts, it moves down and pushes blood out, and because the great vessels hold the heart in place, a mechanism of "cardiac suction" ensues, drawing blood into the atria. As blood fills the atria, the atrial walls stretch and atrial pressure decreases[2,3].

Gravity affects VR by establishing a gradient between the intrathoracic venous compartment and the lower or dependent extremities. For each centimeter below the right atrium, venous pressure increases by about 0.75-0.8 mm Hg. The effect of gravity on venous pressure is such that it causes blood pooling in the legs, and if a person stands quietly for a prolonged period, fainting may occur despite compensatory mechanisms. This effect is due to a reduction in the perfusion pressure of the brain. Venous pressure above the right atrium decreases in the upright position. The pressure in the neck veins is close to 0 mm Hg, and this low pressure causes them to collapse. However, the dural sinuses have rigid walls that prevent their collapse; consequently, they reach subatmospheric pressures (<0 mm Hg).

Muscle contraction facilitates VR by compressing veins. The contractions and relaxation of the muscles surrounding deep veins help push blood upwards. The effect known as the muscle pump accomplish the valves that prevent the blood reflux back into the lower limb, thereby assisting the unidirectional flow of blood into the right atrium[2,3,10].

Venous System Imaging Methods

Venous system, generally, can be presented by selective venography, Doppler sonography, computed tomography (CT) venography (CTV) and magnetic resonance (MR) venography (MRV). Cerebral venous system can be displayed by selective venography, cerebral CTV, cerebral MRV, and specialized extracranial and transcranial Doppler sonography.

Selective venography is an invasive procedure in which the venogram is taken only after a special dye has been injected *via* a catheter into the vein.

CTV reliably reveals all cerebral veins and sinuses when they are seen with MR. Cerebral CTV is superior to MRV in the identification of cerebral veins and dural sinuses and is at least equivalent in the diagnosis of dural sinus thrombosis venography. In addition, CTV more frequently visualizes sinuses or smaller cerebral veins with low flow as compared with MRV. The high-flow draining veins of cerebral and dural arteriovenous malformations, vein of Galen malformation and carotid cavernous fistula are better seen on contrast-enhanced three-dimensional gradient-echo MRV[20].

Venous system can also be presented by using specialized extracranial and transcranial Doppler sonography[11,13]. CCSVI was first found using these methods.

Chronic Cerebrospinal Venous Insufficiency

Chronic cerebrospinal venous insufficiency (CCSVI) describes compromised blood flow in the veins draining the central nervous system. It is hypothesized that it plays a role in the cause of multiple sclerosis (MS)[11-14]. Zamboni *et al.* claimed that in MS patients diagnosed with CCSVI, the azygos and IJV are stenotic in around 90% of cases. They theorize that malformed blood vessels cause increased deposition of iron in the brain, which in turn triggers autoimmunity and degeneration of the nerve myelin sheath[11]. Most of the venous problems in MS patients have been reported to be truncular venous malformations, including azygous stenosis, defective jugular valves and jugular vein aneurysms. Problems with the innominate vein and superior vena cava have also been reported to contribute to CCSVI[14]. The proposed consequences of CCSVI syndrome include intracranial hypoxia, delayed perfusion, reduced drainage of catabolites, increased transmural pressure[15-17], and iron deposits around cerebral veins[18,19]. Multiple sclerosis and other neurodegenerative diseases have been proposed as an outcome of CCSVI. Iron is needed by all living beings. In addition to maintaining cellular balance and enabling nerve cells to perform routine functions, iron forms tissues and blood vessels; it transports oxygen through the body *via* blood circulation; it enables nerve impulses to be transmitted; and it is essential to the development of myelin and oligodendrocytes (which produce and maintain healthy myelin). Iron is deposited in varying amounts in different cells within the body, according to their specific need for proper functioning. While the benefits of iron in normal levels are clear, and even critical for bodily function, conversely, too much stored iron can cause problems. For instance, as people age, iron is more likely to accumulate in the brain. Conditions such as Alzheimer's disease and Parkinson's disease can also occur in connection with iron stores[20].

A randomized controlled study in 499 patients confirmed the prevalence of CCSVI in MS patients that was twice as high as in healthy controls, but this prevalence was also increased, to a lesser extent, in patients with other neurologic diseases[21]. If there is a relationship between CCSVI and MS, it is expected to be a complex one[22-24]. Further investigations are undergoing.

Doppler techniques for evaluation of CCSVI

Cerebral venous circulation can be examined using echo-color Doppler equipped with 2.5 and 7.5 MHz transducers. Usually, physicians evaluate intracranial circulation using transtemporal window. In search for better correlation of the results among different centers and evaluators, the International Society for Neurovascular Disease held a meeting in Bologna in March 2011, where experts discussed the techniques and criteria for CCSVI. There was a consensus opinion that intracranial and extracranial venous circulation can be evaluated by any vascular ultrasound machine through standard transtemporal approach or pterygoidal approach, as suggested by Zamboni *et al.*; the specially created Quality Doppler Profile (QDP) available on Esaote-Biosound machines is helpful in the evaluation of CCSVI, but it is mandatory[11,23].

Each subject has to be investigated first in supine position and then in sitting position (with tilt chair if possible), to detect the following five parameters of the Zamboni protocol[25]:

1. Reflux in the internal jugular veins (IJVs) and/or vertebral veins (VVs) in sitting and supine posture (Figs. 1 and 2a, 2b).
2. Reflux in the intracranial veins. Reflux is defined as a reversal of flow direction during the inspiratory and expiratory phase during normal breathing with mouth closed. The transcranial color-coded duplex sonography (TCCD) studies were carried out using one of two different approaches: the classic transtemporal window or the transcondylar window (Figs. 3 and 4).
3. B-mode evidence of abnormalities in the IJVs, such as stenoses, malformed valve, annulus, septa, etc. (Fig. 5).
4. Flow not Doppler-detectable in IJVs and/or VVs despite numerous deep breaths (Fig. 6).
5. Reverted postural control of the main cerebral venous outflow pathways, detected by measuring the difference in IJV cross-sectional area (CSA) between the supine and upright positions (Fig. 7a, 7b).

Two of the criteria are considered sufficient for the diagnosis of CCSVI[11,13,24,25].

Venous hemodynamics insufficiency severity score (VHISS) is an ordinal measure of the overall extent and number of venous hemodynamics (VH) flow pattern anomalies. A higher value of VHISS indicates greater severity of VH flow pattern anomalies. For each of the five VH criteria, the "VHISS contribution score" can be calculated. These scores combined gave an overall severity measure, i.e. the VHISS. The minimum possible VHISS value is 0 and the maximum is 16.

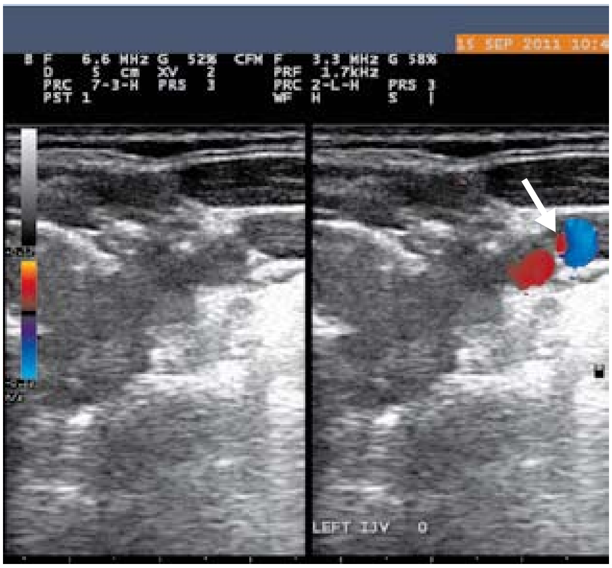


Fig. 1. Reflux (red part of the hemodynamic spectrum in internal jugular vein – blue coded vessel on the right). Red coded vessel on the left is common carotid artery.

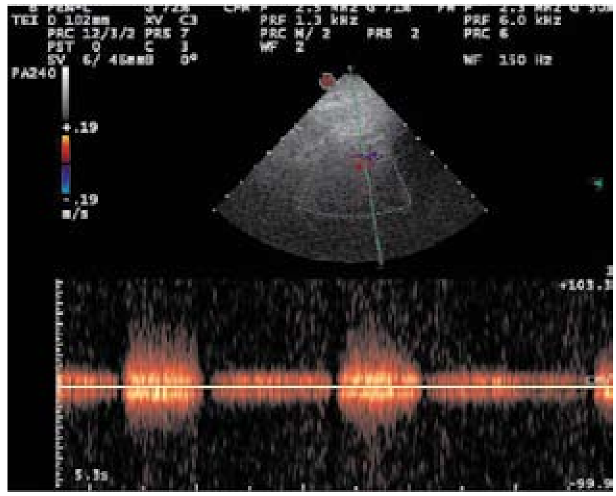


Fig. 3. Transcranial color Doppler of venous circulation, transtemporal approach (Rosenthal vein).

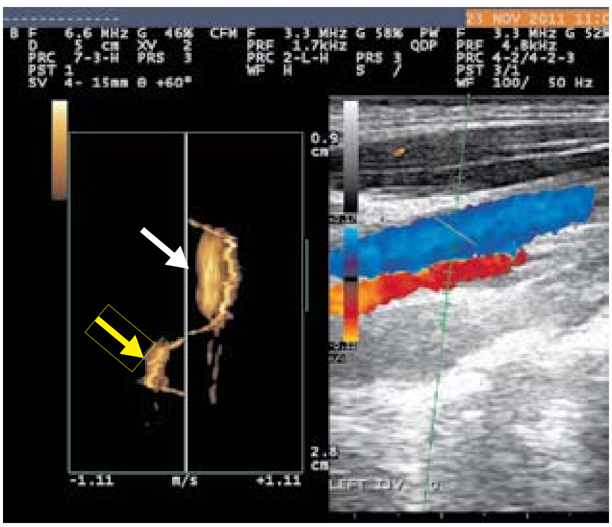


Fig. 2a. Left panel: quality Doppler profile spectrum showing retrograde flow in internal jugular vein (blue coded; white arrow) and anterograde flow in common carotid artery (red coded; yellow arrow).

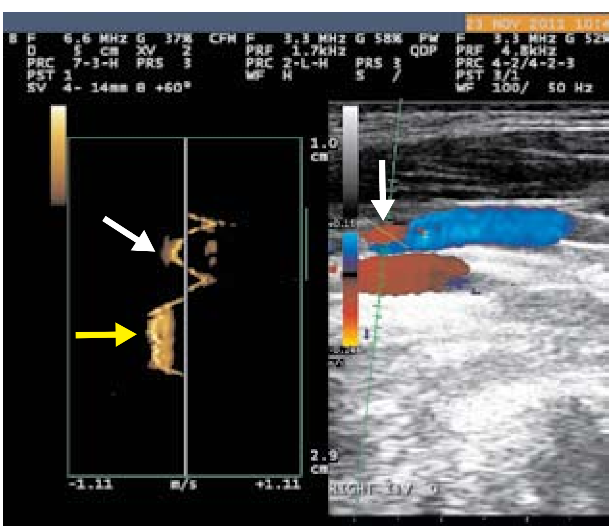


Fig. 2b. Right panel: separation of the quality Doppler profile for internal jugular vein with separation of the color coded flow (white arrow); normal flow in common carotid artery (yellow arrow).

As regards criterion VH1, there are eight venous segments that can potentially exhibit reflux in the two postures, and one point was assigned for each one at which reflux was found to be present. VH1 had a VHISS contribution score that could range from a minimum of 0 to a maximum of 8.

Criterion VH2 was assigned a VHISS contribution score of 1 if reflux was present in the intracranial veins in only one posture and a VHISS contribution score of 2 if it was present in both postures. The VHISS contribution score for this criterion was additionally weighted with a factor of 2 if reflux toward

Fig. 4. Quality Doppler profile of cerebral venous sinuses through transcondylar approach (petrosal sinuses).

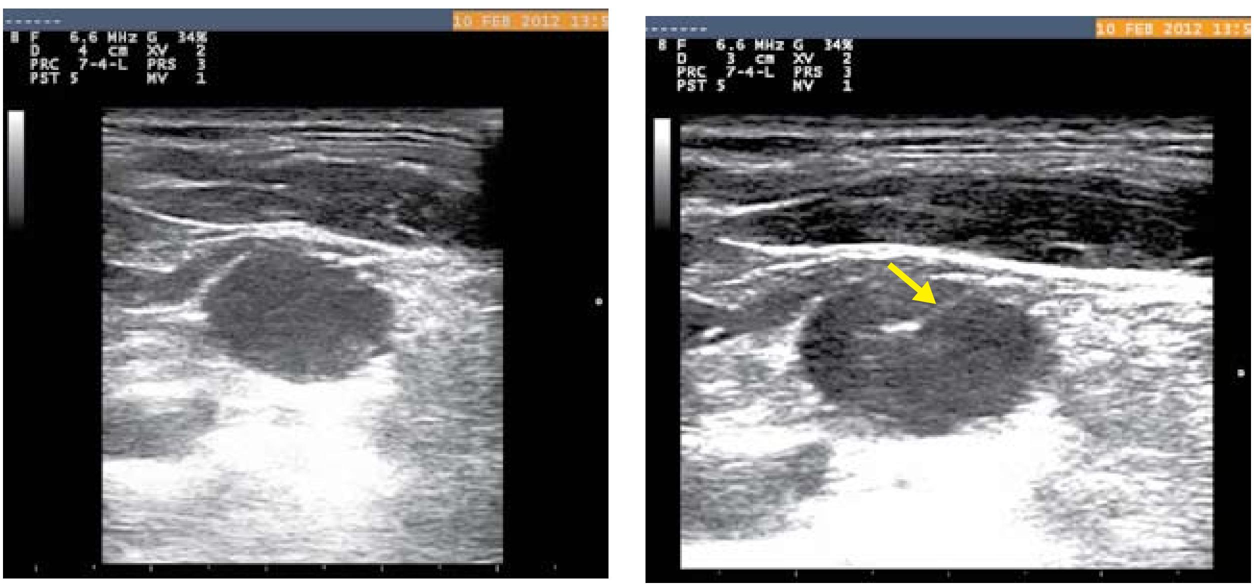


Fig. 5. Left panel: lumen of the vein without any wall defects. Right panel: valve (closed position – yellow arrow).

the subcortical grey matter could be detected. VHISS contribution score for VH2 could range from a minimum of 0 to a maximum of 4.

The VHISS contribution score for VH3 ranged from 0 to 2, depending on whether B-mode anomalies disturbing outflow were present in none, one or both of the IJVs, respectively. VH3 was assigned a contribution score of 0 if either VH1 or VH4 was positive for the presence in either posture of reflux or obstruction in the IJV of interest.

The scoring scheme for the contribution of VH4 to the VHISS was the same as that for VH1, with the difference being that only blocks were considered. No points were assigned for segments and postures in which reflux had previously been detected under VH1.

The VH5 criterion had an overall VHISS contribution score between 0 and 4, calculated by assigning 0 to 2 points for each IJV. A -ΔCSA value was assigned a score of 2, whereas a ΔCSA value <7 mm2,

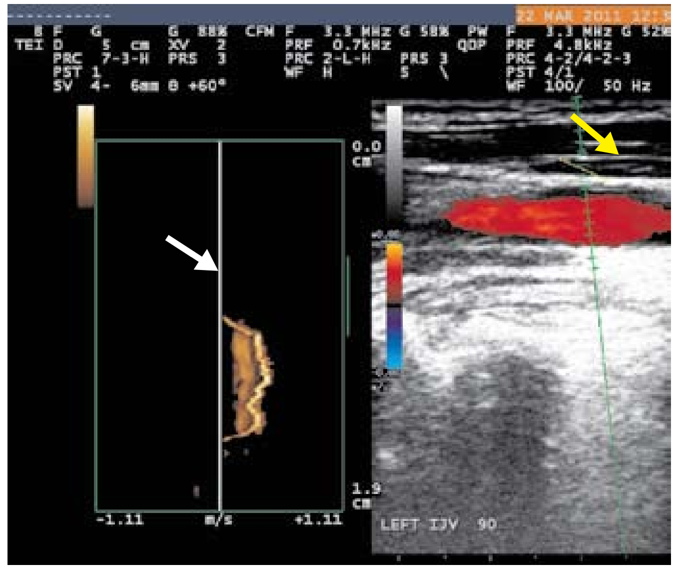


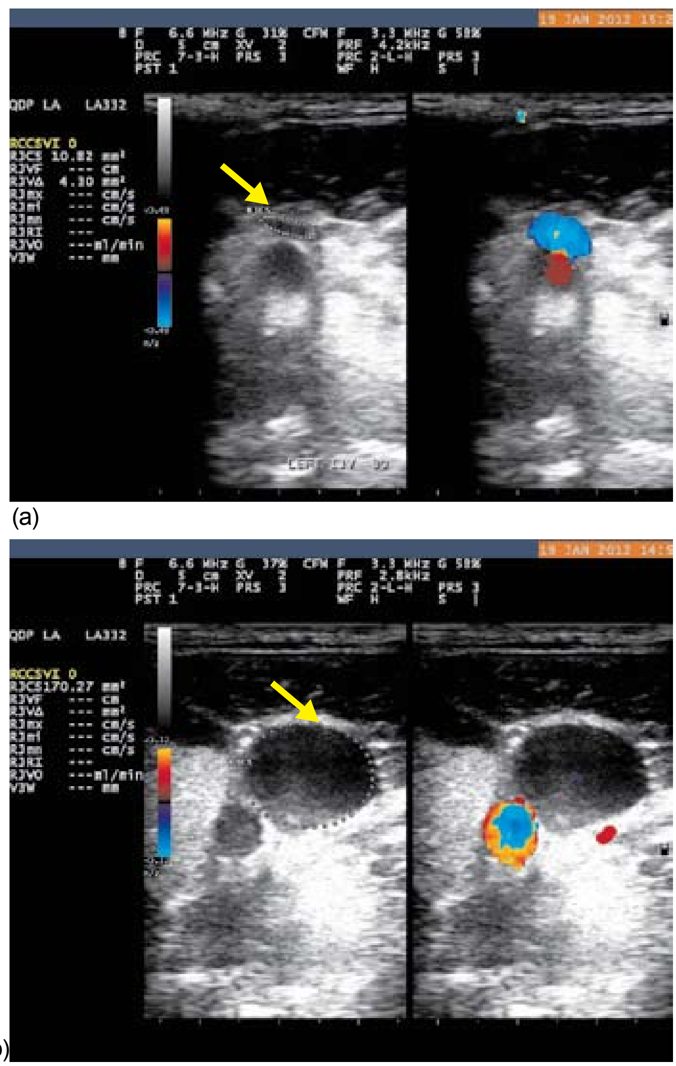
Fig. 6. Absence of color flow and collapsed lumen of internal jugular vein (yellow arrow) and absence of Doppler spectra (white arrow) despite numerous deep breaths.

corresponding to the 25th percentile of ΔCSA distribution in healthy controls, was assigned a score of 1. ΔCSA >7 mm2 was assigned a score of 0.

The overall VHISS score was defined as a weighted sum of the scores contributed by each individual abnormal venous hemodynamics criterion.

It is still not clear whether MRV, venous angiography, or Doppler sonography should be considered the gold standard for the diagnosis of CCSVI[21]. The use of MRV for the diagnosis of CCSVI in MS patients has been proposed by some to have limited value, and should be used only in combination with other techniques[26]. Others have stated that MRV has advantages over Doppler since results are more operator-independent[27].

Evaluation of cerebral venous circulation by means of ultrasound has advantages in correlation with other methods; it is a reproducible, real-time method that provides information on vessel wall morphology and function, as well as on flow characteristics and velocities.



(a)

(b)

Fig. 7. Differences in the internal jugular vein cross section area in supine (a) and sitting (b) position.

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Sažetak

PROCJENA MOŽDANE VENSKE CIRKULACIJE ULTRAZVUKOM

I. Zavoreo, V. Bašić-Kes, L. Zadro-Matovina, M. Lisak, L. Ćorić, T. Cvjetičanin, D. Ciliga i *T. Trošt Bobić*

Venska cirkulacija obuhvaća plućne vene, sistemske vene i venske sinuse prisutne isključivo u lubanji. Cerebralni venski sustav dijeli se u dva glavna dijela, površinski i dubinski cerebralni venski sustav. Glavna zadaća venske cirkulacije je uklanjanje deoksigenirane krvi i štetnih tvari iz tkiva te njihovo odvođenje prema srcu. Vene u usporedbi s arterijama imaju tanju stijenku i veći lumen. U svakom trenu oko 60%-70% ukupnog krvnog volumena u tijelu nalazi se u venama. Glavni čimbenici koji utječu na funkciju venskog sustava su respiracijski ciklus, tonus vena, funkcija desne strane srca, gravitacija te funkcija mišićne pumpe. Venska cirkulacija se, općenito, može prikazati invazivnom metodom selektivne venografije i neinvazivnim metodama dopler sonografije, CT venografijom i MR venografijom. Cerebralni venski sustav prikazuje se selektivnom venografijom, moždanom CT venografijom, moždanom MR venografijom i specijaliziranom intrakranijskom i ekstrakranijskom dopler sonografijom. Cilj ovoga rada je opisati mogućnosti prikazivanja venske cirkulacije glave i vrata pomoću metoda ultrazvučnog prikaza, naročito kronične venske insuficijencije kao jednog od najčešćih patofizioloških entiteta koji se povezuju s nastankom neurodegenerativnih bolesti.

Ključne riječi: *Vene – radiografija; Vene – ultrazvuk; Moždane vene – ultrazvuk; Cerebrovaskularni poremećaji; Kronična cerebrospinalna venska insuficijencija; Transkranijska dopler sonografija; Zambonijev protokol*