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From pathophysiology to symptoms of chronic cerebrospinal venous insufficiency

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Abstract

Chronic Cerebrospinal Venous Insufficiency (CCSVI), and its variant limited to the internal jugular veins, is a multifactorial condition characterized by reduced extracranial venous outflow due to valvular abnormalities, intraluminal lesions, structural anomalies, and extrinsic compressions. This results in dysfunction of the glymphatic system with cerebrospinal fluid stasis, increased intracranial pressure, and cerebral hypoperfusion.

The objective of this study was to collect and integrate all symptoms potentially caused by CCSVI and to explain the underlying pathophysiological mechanism.

A systematic analysis of the recent literature concerning CCSVI was performed, focusing on the anatomical causes, diagnostic evaluation (Color Doppler Ultrasound, CDUS; Computed Tomography, CT angiography; Magnetic Resonance, MR venography; catheter venography; Single-Photon Emission Computed Tomography, SPECT/CT), and the clinical implications of reduced extracranial venous outflow.

The alteration of venous outflow through the internal jugular veins leads to intracranial hypertension, cerebral hypoperfusion, and dysfunction of the glymphatic system with stagnation of cerebrospinal fluid.

These mechanisms determine a heterogeneous symptomatologic picture that includes dysesthesia, ipsilateral facial pain, morning soft tissue swelling, vertigo, hypoacusis, diplopia,

headache, chronic fatigue, and bladder control disorders, as well as other related symptoms. Scientific evidence also shows symptomatic improvement following angioplasty or autologous venous stenting.

CCSVI is a multifactorial syndrome that requires both a multimodal diagnostic approach and a multidisciplinary therapeutic strategy.

Key words: CCSVI, symptoms, headache, vertigo, visual disturbance.

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Introduction

Cerebral venous drainage is primarily mediated by the internal jugular veins and the vertebral venous plexus, which constitute the main extracranial venous outflow routes.

Chronic Cerebrospinal Venous Insufficiency (CCSVI) is a condition characterized by restricted cerebral venous outflow due to valvular abnormalities (immobile or defective valve leaflets),[1] intraluminal obstacles, or muscular/skeletal compressions[2] that affect the Internal Jugular Veins (IJV) and/or the azygos veins, causing a slowing of flow at the level of the IJV and an increase in blood volume in the collateral vessels.[3-4]

From a clinical standpoint, the jugular vein can be divided into three segments: the J3 (superior) segment is located anatomically at the carotid bifurcation, *i.e.*, at the level of the mandibular angle; the J2 (middle) segment is at the level of the thyroid lobe and the ipsilateral cricoid cartilage; and, finally, J1 (the inferior segment) corresponds to the level at which it drains into the brachiocephalic venous trunk.[5]

A normal IJV gradually reduces its longitudinal diameter from J1 to J3,[6] and flow physiologically tends to increase in volume from J3 to J1,[7] both under basal conditions and when the thoracic pump is activated.

This was confirmed by the work of Mohammed *et al.* (2019), in which they analysed cerebral venous drainage through the jugular veins using Color Doppler Ultrasound (CDUS) and confirmed the progressive increase in flow velocity and cross-sectional area from the cranial to the caudal segments.

Furthermore, this study highlighted the IJV as the main route of cerebral outflow in the supine position and in conditions of increased intracranial venous return.[8]

The alterations that lead to a reduction in cerebral venous flow in CCSVI are: i) valvular obstacles, elongated, immobile valve leaflets arranged longitudinally in the IJV, usually at the level of J1; ii) external compressions: when anatomical structures such as the omohyoid muscle

(usually at J2), the styloid process (at J3), or an elongated transverse process compress the IJV; iii) structural alterations such as the presence of endoluminal septa, hypoplasia - the vein has long venous segments that are underdeveloped and of negligible calibre, torsion - referring to the presence of severe stenoses resulting from a venous segment twisted around its own axis, membranous obstruction - when there is an abnormal membrane that almost completely occludes a vein, agenesis - referring to the complete anatomical absence of a venous segment.[9] These mechanisms lead to a significant reduction in flow through the IJV, with a consequent compensatory increase in flow through collateral vessels (measured as the collateral flow index, CFI), which may rise to as much as 65-70%[10] compared with normal values.

The main collateral drainage pathways include the external jugular vein, anterior jugular vein, facial vein, superior thyroid vein, and the vertebral venous plexus (Figure 1).

It is essential to distinguish stenosis from congenital hypoplasia, in the latter, collateral vessels appear normal due to a well-compensated system, whereas in acquired stenosis, collateral circulation becomes augmented, and patients typically become symptomatic.[11]

It is important to emphasize that CCSVI almost never has a single cause.

In most cases, the clinical picture is the result of a combination of different pathogenetic mechanisms (for example, valvular anomalies associated with extrinsic compressions or with structural alterations of the vessel); this is why the ISNVD recommends the use of a multimodal imaging approach, both non-invasive and invasive, to optimally identify extracranial venous structural/morphological and haemodynamic/functional abnormalities indicative of CCSVI.[12]

Simka *et al.* (2021), through fluid dynamic simulations of jugular flow, demonstrated that valvular alterations alone were not sufficient to explain the reduction of venous flow observed in CCSVI, whereas the combination of cranial stenoses and extrinsic compressions had a more significant impact on jugular flow velocity and pressure, thus confirming the multifactorial origin of CCSVI.[13]

Each diagnostic tool has specific advantages, but if used in isolation it offers only a partial view of the overall haemodynamic picture.

It is only through the integration of multiple methods that a complete and reliable assessment of the cerebral venous condition can be obtained.

CDUS represents the first-line tool: it is non-invasive, dynamic, and allows not only identification of intraluminal obstacles (such as dysfunctional valves or septa), but also assessment of their haemodynamic impact, both in the supine and the orthostatic position. CDUS is also the only method capable of detecting functional valvular abnormalities, which are found mainly at the level of J1.

These situations are uniquely present in Duplex evaluation and, moreover permit patient's respiratory participation upon demand.

However, CDUS has certain limitations, particularly in the morphological and spatial assessment of bony or muscular compressions and moreover is severely operator-dependent.

In such cases, Computed Tomography (CT) angiography and Magnetic Resonance Venography (MRV) prove indispensable, thanks to their ability to provide detailed three-dimensional reconstructions of the course of the jugular veins and the surrounding structures.

Nevertheless, CT angiography and MRV are not without limitations, as they are generally acquired only in the supine position and provide a static assessment, without the possibility of evaluating dynamic haemodynamic changes, postural variations, or active patient participation during the examination.

Their usefulness has clearly emerged in the identification of the bony “nutcracker” in the jugular variant of Eagle syndrome, which cannot be assessed with CDUS alone.

Catheter venography, although an invasive method, is considered the gold standard in the pre-interventional phase because it not only allows diagnostic confirmation of a stenosis but also enables immediate treatment, such as balloon angioplasty.

It is useful when non-invasive examinations are inconclusive or discordant with one another, or when an endovascular treatment is being planned.

Finally, the use of Single-Photon Emission Computed Tomography / Computed Tomography (SPECT/CT) is also important; it is fundamental especially for quantifying cerebral hypoperfusion, thus providing a further objective parameter of circulatory impairment secondary to CCSVI, and it is particularly useful in postoperative monitoring.

Symptoms

A prospective study conducted by Bavera *et al.* (2015) on a sample of 366 patients followed for four years by Duplex monitoring identified the most frequent symptoms as: diplopia, fatigue, headache, numbness and reduced mobility of the upper and lower limbs, altered thermal sensitivity, bladder control disorders, impaired coordination and balance, poor sleep quality, dizziness, and difficulty concentrating.[14]

The study by Da Zhou *et al.* (2018) examined 43 patients: 29 had unilateral IJV stenosis, and the remaining 14 had bilateral IJV stenosis.

The common clinical symptoms at admission were tinnitus (60.5%), tinnitus cerebri (67.6%), headache (48.8%), dizziness (32.6%), visual disorders (39.5%), hearing impairment (39.5%), neck discomfort (39.5%), sleep disturbance (60.5%), anxiety or depression (37.5%) and subjective memory decline (30.2%).

Eighteen patients with IJV stenosis related to a venous wall anomaly underwent endovenous stenting, their associated symptoms and signs significantly improved or resolved post-procedure.

In contrast, the other 25 patients in this cohort, who did not receive stenting, reported persistent or even worsening of these symptoms during a clinical follow-up of 0.5 to 2.5 years.

Elevated intracranial pressure is also a fundamental symptom, indeed among the 43 patients, 34 underwent lumbar puncture to quantify intracranial pressure.

Severe intracranial hypertension (>250 mmH2O) was detected in 15 individuals, mild to moderate hypertension in 6, while the remaining 13 subjects exhibited normal intracranial pressure.[15]

Furthermore, a subsequent study by Da Zhou investigated 15 symptomatic patients with idiopathic intracranial hypertension that was unresponsive to pharmacological therapy, assessed by fundoscopy and lumbar puncture.

In all these patients, a non-thrombotic stenosis of the IJV at the J3 segment was identified, later confirmed by digital subtraction angiography.

The most prominent clinical symptoms of IJV stenosis in this study were as follows: headache 100% (15/15), head noise or tinnitus 73.3% (11/15), which is the most characteristic symptom of IJV stenosis, and visual impairment 80% (12/15), such as vision loss 25% (3/12), blurred vision 66.7% (8/12) and dysmorphopsia 41.7% (5/12).

All 15 patients underwent endovascular stenting, and in this cohort as well, the collateral circulation resolved immediately, with all symptoms improving within one week.[16]

An important contribution also derives from research on clinical pictures related to CCSVI. Among the possible causes of CCSVI is the jugular variant of Eagle syndrome, a condition characterized by elongation of the styloid process and/or calcification of the stylohyoid ligament, which may result in compression of the internal jugular vein.[17]

Zamboni *et al.* (2019), for example, analysed the most recurrent symptoms in Eagle syndrome, one of the possible causes of CCSVI, finding as the main manifestations: headache, numbness, dizziness, ipsilateral facial oedema, ipsilateral pain, and episodes of non-aneurysmal perimesencephalic subarachnoid haemorrhage.[17]

The symptomatology of CCSVI also involves chronic fatigue, which represents one of the most disabling manifestations.

In a pilot longitudinal study, Malagoni *et al.* (2010) evaluated the effect of venous angioplasty in patients with multiple sclerosis and CCSVI, finding a significant improvement in chronic fatigue, measured with the "Fatigue Severity Scale" and the "Modified Fatigue Impact Scale", both at 1 and at 12 months after treatment.

These data suggest that chronic fatigue is plausibly a symptom directly linked to CCSVI.[18]

Finally, Beggs *et al.* (2018) investigated, in patients with multiple sclerosis and obstruction of the IJV, the impact of balloon angioplasty.

The study showed a significant and lasting improvement in headache, which is the symptom most frequently reported by patients together with fatigue.[19]

We can therefore readily understand how this condition may present with a very heterogeneous symptomatological picture, with symptoms that differ markedly from one another in site and in mode of onset.

In reality, these clinical manifestations are all caused by common pathophysiological mechanisms of CCSVI, because obstruction to cerebral venous outflow generates a cascade effect that involves the glymphatic system, cerebral perfusion, intracranial pressure, and the neurosensory system.

In light of this, we shall analyse various symptoms to highlight how they all share a common origin attributable to CCSVI, thereby reinforcing the hypothesis that the latter, instead of being an isolated anatomical condition, is a multifactorial pathological condition.

Pathophysiology

Dysaesthesias and alterations in thermal sensitivity may be attributed to dysfunction of the glymphatic system and reduced cerebral perfusion, or to a simple elongated styloid process that compresses nerve endings.

Under conditions of CCSVI, venous obstruction determines an upstream increase in venous pressure and a stasis of cerebrospinal fluid, hindering the proper drainage of waste substances from the cerebral parenchyma (Figure 2).[20]

This accumulation of toxic metabolites, together with cerebral hypoperfusion consequent to the increase in intracranial pressure, leads to phenomena of inflammation and oxidative stress that cause progressive damage to sensory neurones, thereby generating dysaesthesia and alteration of the neurosensory system.[21]

The study by Shaykevich S. *et al.* (2022) confirms that, in cases of CCSVI, dysfunction of the lymphatic system leads to an accumulation of neurotoxic metabolites that impairs cognitive functions, and that the best non-invasive diagnostic tool to assess this dysfunction is functional optoacoustic neuro-tomography as it allows in vivo mapping of perivascular pathways and metabolic clearance.[22]

The dilation of perivascular spaces represents an indirect sign of impaired venous outflow, as demonstrated by the study of Li *et al.*[23]

Ipsilateral facial pain, on the other hand, can be explained by the involvement of the dura mater, which is richly innervated by afferent fibres arising from the trigeminal ganglion, particularly the spinal nerve, which is a branch of the mandibular nerve (Figure 3).[24]

In the presence of CCSVI, the increase in venous pressure within the dural venous sinuses, especially in the superior sagittal sinus, may lead to a distension or mechanical compression of these meningeal nociceptors.

This abnormal stimulation of trigeminal fibres can generate pain radiating along the territories innervated by the nerve itself, manifesting clinically as unilateral facial pain.

Soft-tissue swelling is caused by several interconnected pathological mechanisms.

First, obstruction of outflow through the IJV entails an increase in hydrostatic pressure in the upstream venous capillaries; this rise in pressure favours the extravasation of fluid from the vascular compartment into the interstitium, contributing to the formation of oedema.

Moreover, in cases of IJV obstruction the external jugular vein is often recruited as a collateral pathway and is therefore subjected to a greater, non-physiological haemodynamic load, which results in a further increase in superficial venous pressure and thus an aggravation of the oedema.

A second factor involved is the lymphatic system, whose primary function is precisely the drainage of interstitial fluids; if this system is altered, there will be a worsening of the oedema.

Finally, soft-tissue swelling is especially a morning phenomenon, since in the supine position venous drainage occurs almost exclusively through the IJV and, accordingly, if the latter is obstructed there will be an increase in upstream pressure.[25-27]

In addition, in the supine position the accumulation of fluids in the soft tissues is further promoted by the absence of the gravitational effect (Figure 4).

Nuchal and orbital headache in patients with CCSVI may be attributed to increased intracranial pressure secondary to cerebrospinal fluid stasis.

Unlike other organs, cerebral perfusion pressure does not depend solely on mean arterial pressure but must also take intracranial pressure into account:

Perfusion pressure = Mean arterial pressure - Intracranial pressure

Thus, increasing intracranial pressure would lead to cerebral hypoperfusion (Figure 5).[28]

Moreover, venous congestion may involve the vascular structures of the occipital and cervical regions, which irritate the occipital nerves, thereby generating an occipital neuralgia, a particular nuchal pain that radiates to the orbital region.

Vertigo is caused mainly by increased venous pressure in the superior petrosal sinus, because it is the principal structure responsible for draining the inner ear.

In reality, the inner ear is drained by the auditory vein (when present) and by the vein of the vestibular aqueduct, which in turn drain into the superior petrosal sinus, whereas the vein of the cochlear aqueduct drains directly into the superior bulb of the IJV.

The increase in venous pressure at the level of the superior petrosal sinus hampers outflow from the microcirculation of the inner ear, damaging structures such as the stria vascularis, the utricle, and the saccule, which are essential for balance and ionic homeostasis.

The result is the detachment of otoliths from their seats, which then migrate into the semicircular canals, triggering the typical episodes of benign paroxysmal positional vertigo.[29]

Toro *et al.* (2018) developed a computational model demonstrating how extracranial outflow stenosis can alter pressure gradients within the inner ear fluids, leading to endolymphatic hydrops and damaging the stria vascularis.[30]

In support of this concept, Alpini *et al.* (2016) investigated the potential association between CCSVI and Ménière disease, suggesting that impaired venous outflow may create the anatomical and haemodynamic conditions favouring the development of endolymphatic hydrops.[31]

Hearing loss and tinnitus can be explained by this mechanism, because damage to the stria vascularis prevents the entry of K^+ ions into the endolymph, leading to a reduction in the endolymphatic potential (physiologically around 80 mV), thereby preventing the hair cells located in the Organ of Corti from depolarizing when stimulated by sound vibrations.[32]

In 2014, Bruno A. *et al.* conducted a study on 50 patients with Ménière's disease (MD), evaluating, through CDUS and phlebography, the relationship between MD and CCSVI.

Of the 50 patients, 45 tested positive for at least two diagnostic criteria for CCSVI, and of these, 20 were treated with catheter venography, with a significant improvement in symptoms in 90% of cases.[33]

Menegatti *et al.* (2017) also demonstrated that individuals diagnosed with both multiple sclerosis and inner ear disorders exhibited a higher prevalence of CCSVI, with both groups showing an increased incidence of valvular abnormalities in the IJV compared to healthy participants.[34]

Further confirmation of this mechanism is provided by the study of Di Stadio *et al.* (2025), which examined two patients with tinnitus but without associated balance disorders.

An MRV evaluation was performed on these patients, and it was observed that one patient presented a stenosis of the transverse sinus, the sigmoid sinus, and the ipsilateral carotid artery, while the other patient showed only a stenosis of the right transverse sinus without contralateral compensatory hyperplasia.

The authors concluded that these tinnitus cases may be due to an alteration of venous flow, which causes hydrops and reduces the elimination of reactive oxygen species, resulting in damage to the hair cells and the onset of tinnitus.[35]

Visual disturbances, on the other hand, are mainly caused by an increase in intracranial pressure, which leads to optic nerve dysfunction, or they may result from a venous infarction in the occipital cortex, or they may be caused by extensive venous infarctions or uncal or tonsillar herniations that produce a mass effect on the occipital arteries.[36]

An example of the latter case is the study by Fiona J. *et al.* (2012), which describes two patients with visual disturbances affected by idiopathic intracranial hypertension, subsequently treated with lumboperitoneal or ventriculoperitoneal shunts, and in both cases, as a complication, the formation of cerebellar tonsillar herniations occurred, compressing the sixth cranial nerve.[37]

Intracranial pressure affects the optic nerve, since the cerebrospinal fluid originating from the intracranial subarachnoid space flows into the sheath of the optic nerve through the chiasmatic cistern.[38]

The elevated cerebrospinal fluid pressure within the intracranial subarachnoid space is transmitted along the sheath of the optic nerve toward its retrobulbar region, influencing the normal gradient between intraocular and intracranial pressure.[39]

Consequently, the pressure within the retrolaminar portion of the optic nerve increases, impairing axoplasmic transport, inducing flow stasis, and leading to axoplasmic accumulation within the lamina cribrosa, thereby causing papilledema.[40]

The retrolaminar blood vessels, including the posterior ciliary arteries, are compressed by the elevated pressure within the subarachnoid space of the optic nerve sheath.[41]

In support of this hypothesis Adamczyk-Ludyga *et al.* (2012) analyzed retinal and optic nerve parameters in patients with multiple sclerosis, with and without CCSVI.

By combining optical coherence tomography with catheter venography, the authors demonstrated that patients with jugular outflow obstruction exhibited a reduction in retinal nerve fibre layer thickness and microcirculatory alterations consistent with orbital venous congestion.

In the initial phase, when venous pressure increases and cerebrospinal fluid accumulates around the optic nerve, the fibres swell, causing a slight thickening of the retinal nerve fibre layer and papilledema.

However, if this impaired drainage persists, the reduced tissue oxygenation induces axonal stress and hypoxia, leading progressively to loss and thinning of the retinal nerve fibres.

Consequently, the reduction in retinal nerve fibre thickness observed in chronic cases is not a sign of low intracranial pressure, but rather represents the late stage of prolonged venous and perioptic congestion.[42]

Moreover, the increase in cerebrospinal fluid pressure also induces an increase in central retinal venous pressure, reducing retinal perfusion pressure,[43] because unlike cerebral perfusion pressure, the orbital perfusion depends on:

Retinal perfusion pressure = P retinal artery - P retinal vein - P orbital

Chronic fatigue, difficulty concentrating, and reduced sleep quality are the most disabling symptoms of CCSVI and derive from cerebral hypoperfusion consequent to increased intracranial pressure.

This process generates widespread functional impairment, but it is particularly marked at the level of the basal ganglia, such as the caudate nucleus and the substantia nigra, which are central areas in the control of tone and motivation.

These structures are located deep within the brain parenchyma and are relatively distant from the main venous outflow pathways, which renders them more exposed to the rise in pressure and therefore to greater suffering related to hypoperfusion.

For bladder control disorders, it is useful to recall the study by P. Zhao *et al.* (2023), which investigated urinary dysfunction in patients with Vascular Cognitive Impairment (VCI). [44]

The authors observed that the onset of urinary incontinence is strongly associated with alterations in the perfusion of the frontal areas, responsible for the voluntary inhibitory control of micturition, and with altered perfusion of the pontine micturition centre, which coordinates the descending pathways to the spinal cord.

This study therefore shows that haemodynamic or ischaemic damage in these critical regions is sufficient to compromise the delicate balance between voluntary control and automatic reflexes, resulting in urinary urgency and incontinence.

Griffith *et al.* (2015) likewise demonstrate that the spino-bulbo-spinal reflex mediated by the pontine micturition centre underpins active control of micturition, and that the periaqueductal

grey is the “switch” that induces micturition and maintains a strong connection with the prefrontal lobe.[45]

In light of such evidence, it is plausible to hypothesise that similar mechanisms may operate in CCSVI: chronic hypoperfusion and cerebral venous congestion could affect fronto-subcortical circuits and especially the pontine centre, leading to a reduced ability to modulate sacral reflex activity and consequent urinary dysfunction.

Moreover, in the study by Di Filippo *et al.* (2014), urinary incontinence was observed even in the early stages of multiple sclerosis, a pathology that shows a close association with CCSVI.[46] This finding strengthens the hypothesis that bladder disorders may be interpreted as an early and direct manifestation of the haemodynamic and neurovascular alterations typical of CCSVI.

CCSVI can also cause non-aneurysmal perimesencephalic subarachnoid haemorrhage, since the increase in upstream venous pressure may also involve the veins of Rosenthal, causing them to rupture.

This mechanism is particularly critical in variants B and C of the veins of Rosenthal, because in this case they do not drain directly into the galenic system, which predisposes them to rupture (Figure 6).[47]

Lifestyle factors in Chronic Cerebrospinal Venous Insufficiency

Lifestyle-related factors may influence the clinical expression and symptoms burden of CCSVI, although the disorder is primarily defined by structural and haemodynamic abnormalities of the extracranial venous outflow pathways.

Among these factors, obesity and recent weight gain appear to be the most relevant.

Central obesity leads to increased intra-abdominal pressure, with a consequent rise in both pleural and cardiac filling pressures, thereby hindering venous return from the brain and playing a key role in the onset and recurrence of idiopathic intracranial hypertension.[48]

In this regard, the study of Sinclair AJ *et al.* enrolled 25 overweight patients with idiopathic intracranial hypertension who were placed on a low-energy diet; after 3 months, these patients showed significant reductions in intracranial pressure, improvement of symptoms, and a decrease in optic disc swelling.[49]

Wills *et al.* further confirmed this concept: in their study, 97 obese patients with idiopathic intracranial hypertension underwent bariatric surgery, resulting in reduction of intracranial pressure together with significant improvement in headache, papilloedema, visual field deficits, and visual symptoms. [50]

Therefore, this aspect may be particularly relevant in patients with jugular outflow disturbance who also present with symptoms commonly observed in intracranial hypertension, such as headache, visual disturbances, pulsatile tinnitus, and fatigue.

It has also been suggested that obesity might be correlated with calcification of the stylohyoid complex; however, this association was not confirmed by a study of Al-Amad SH, *et al.*[51]

Sleep may represent a second important modifiable domain.

Karam et al. reported in their systematic review and meta-analysis that, a cohort of 319 patients with idiopathic intracranial hypertension, 42% suffered from sleep disorders, particularly obstructive sleep apnea.[52]

Indeed, sleep disturbances are increasingly recognized in patients with idiopathic intracranial hypertension, and obstructive sleep apnea may further worsen the clinical picture by altering nocturnal respiratory dynamics, venous return, and intracranial pressure regulation, while also contributing to headache burden, fatigue, and reduced quality of life.

Moreover, the glymphatic system is particularly active during slow-wave sleep, whereas sleep disorders are associated with the reduction of this wave.[53]

This may result in impairment of glymphatic function and altered drainage of cerebrospinal fluid and other waste products from the brain, thereby contributing to increased intracranial pressure.[53]

Therefore, since weight management remains a central therapeutic strategy in conditions characterized by raised intracranial pressure, lifestyle measures aimed at achieving a negative energy balance, including dietary intervention and regular physical activity, may be regarded as relevant components of a broader management approach.

Conclusions

CCSVI and its variant limited to the IJV represent complex, multifactorial conditions, characterised by a slowing of cerebral venous outflow and the activation of compensatory mechanisms via collateral vessels.

Structural and functional alterations of the IJV, associated with external compressions and valvular anomalies, determine an increase in upstream venous pressure, with consequent cerebrospinal fluid stasis, alteration of the glymphatic system, increased intracranial pressure, and cerebral hypoperfusion.

These pathophysiological changes generate a heterogeneous clinical picture, suggesting that CCSVI should not be regarded merely as an anatomical condition, but rather as a multifactorial pathology that requires a multidisciplinary diagnostic and therapeutic approach.

Within this broader framework, modifiable systemic and lifestyle-related factors should also be taken into consideration, as they may influence both symptom severity and clinical course.

In particular, body weight and sleep quality may contribute to amplifying the haemodynamic and intracranial consequences of impaired venous outflow.

Therefore, correction of these factors may reasonably be considered part of a comprehensive and individualized terapeutic strategy, alongside the anatomical and haemodynamic assessment of venous obstruction.

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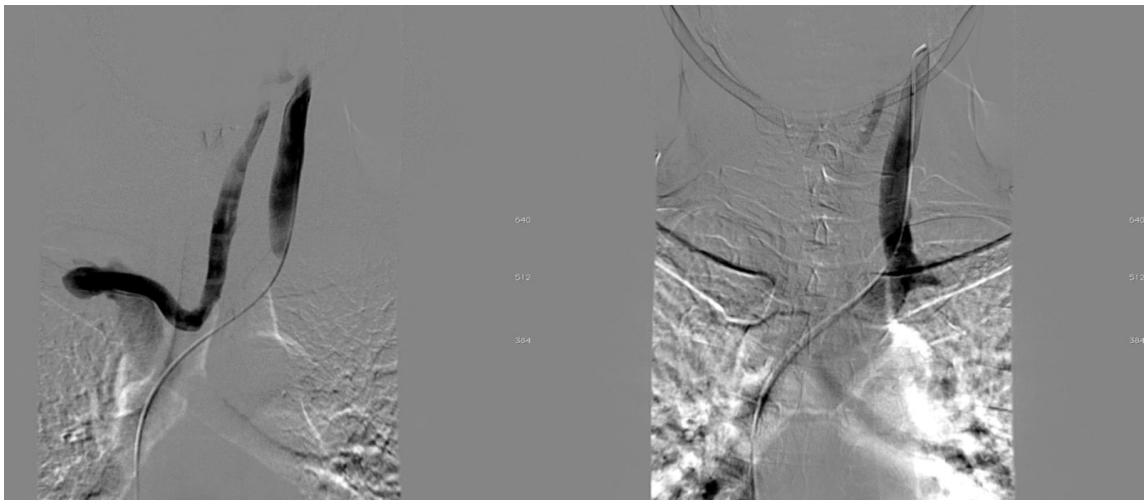

Figure 1. collateral vessels before angioplasty (left panel) and after angioplasty (right panel).

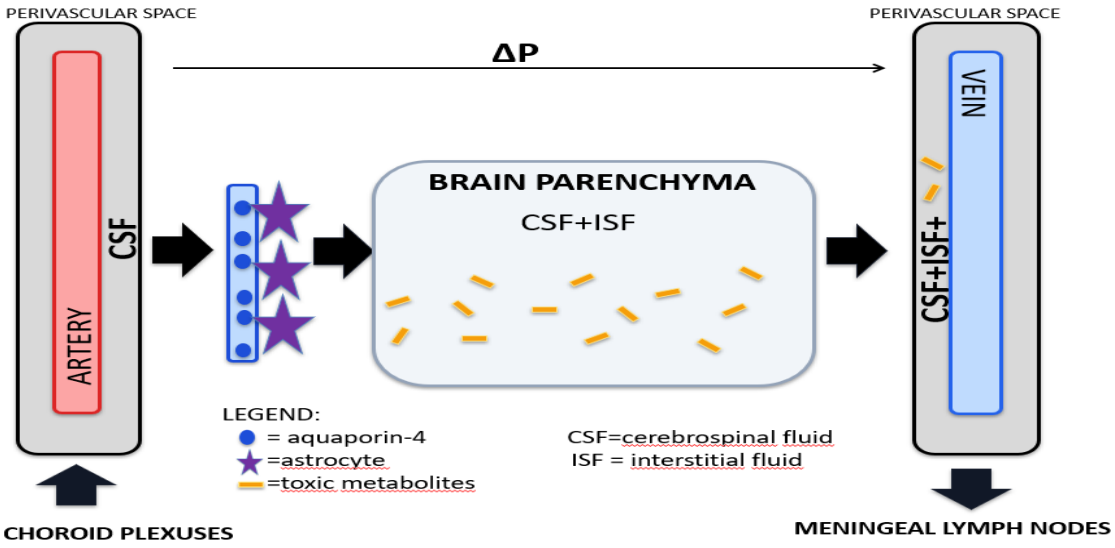

Figure 2. Glymphatic system.

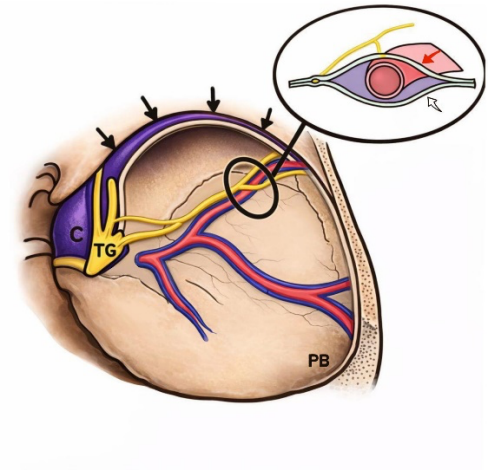

Figure 3. Topographical diagram of the vascular conflict between petrous body (PB), the trigeminal ganglion (yellow), the middle meningeal artery (red), the middle meningeal vein (blue), the sphenoparietal sinus (black arrow), the cavernous sinus (C), meningeal layer of the dura mater (red arrow), periosteal layer of the dura mater (black arrow).

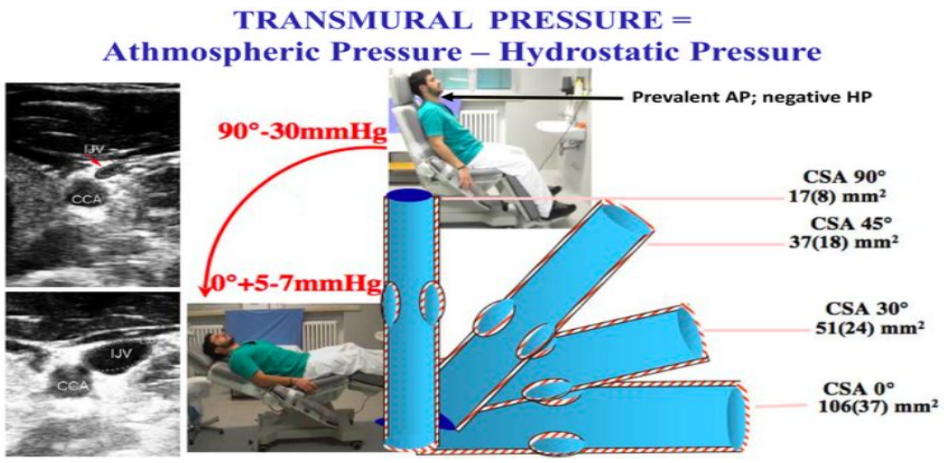

Figure 4. This image shows that head-up tilt reduces transmural pressure and collapses the internal jugular vein, with cross-sectional area (CSA) decreasing from 106→51→37→17 mm² at 0°, 30°, 45°, and 90°, respectively.[27]

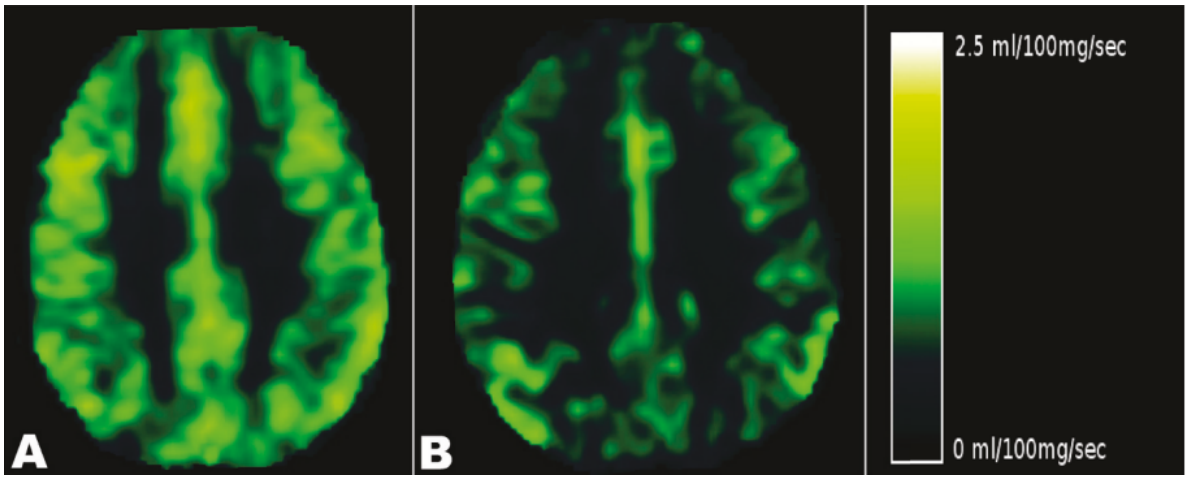

Figure 5. Left: cerebral blood flow (CBF) in a 33-year-old patient with relapsing–remitting (RR) multiple sclerosis (MS) and chronic cerebrospinal venous insufficiency (CCSVI). Right: CBF in a 38-year-old patient with RR MS and CCSVI.[28] In both cases, a marked reduction in cerebral perfusion can be observed.

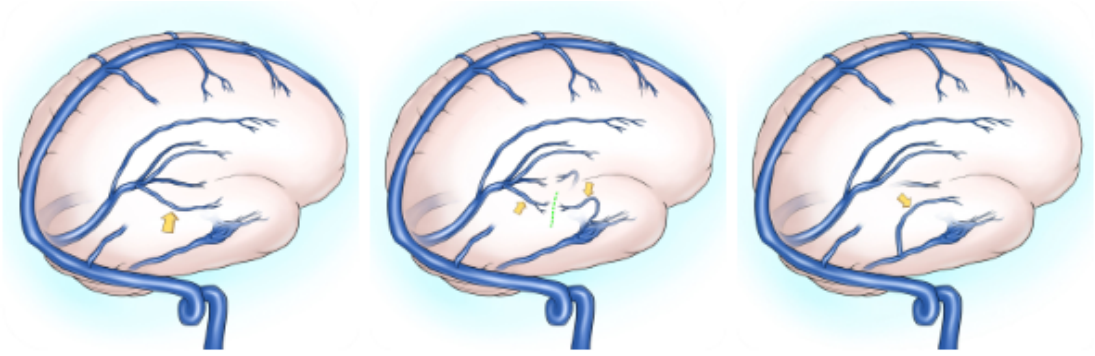

Figure 6. Anatomical variants of the veins of Rosenthal. Yellow arrows indicate the veins of Rosenthal; red arrows indicate the vein of Galen; blue arrows indicate the straight sinus.