Review

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# Diagnostics and Treatment of Cerebral Venous Thrombosis

***G.R. Ramazanov, Kh.V. Korigova✉, S.S. Petrikov***

**Neurological Department for Patients with Acute Cerebrovascular Accidents**
**N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department**
**3 B. Sukharevskaya Sq., Moscow, 129090, Russian Federation**

✉ **Contacts:** Khedi V. Korigova, Neurologist, Neurological Department for Patients with Acute Cerebrovascular Accidents, N.V. Sklifosovsky Research Institute for Emergency Medicine.

Email: khadi.korigova@mail.ru

**BACKGROUND**

This article is devoted to the discussion of a life-threatening and difficult to diagnose disease — cerebral venous thrombosis (CVT). The article lists clinical manifestations, features of diagnosis and treatment of CVT. Cerebral venous thrombosis is an emergency that requires a quick decision to start therapy in order to prevent the development of venous cerebral infarction, intracranial hemorrhage, severe disability and death. Cerebral venous thrombosis is a rare and rather difficult to recognize form of acute cerebrovascular accident (ACVA). Considering the variability of the clinical and radiological picture, as well as the large number of risk factors, CVT is a complex medical problem. Despite the fact that CVTs account for less than 1% of all ACVA, significant differences in treatment necessitate the earliest possible differential diagnosis of CVT with arterial stroke. The diagnosis is often made with a delay due to a wide range of clinical manifestations, subacute onset of the disease, as well as low alertness of specialists in relation to CVT. In patients with cryptogenic stroke, CVT should be ruled out as a potential cause of stroke. Among other things, in the case of CVT, as in the case of thrombosis of the cerebral arteries, the establishment of the leading etiological factor is one of the priority tasks, the solution of which allows choosing the optimal means of secondary prevention.

**AIM OF STUDY** Raising awareness of doctors of multidisciplinary hospitals about clinical manifestations, methods of diagnosis and treatment of CVT.

**MATERIAL AND METHODS** To achieve this goal, the results of domestic and foreign scientific research on the diagno-sis and treatment of CVT were analyzed. Literature searches were carried out in electronic search engines Scopus, eLibrary, PubMed using the keywords: cerebral venous thrombosis, cryptogenic stroke, intracerebral hemorrhage, anticoagulant therapy, neurological imaging in cerebral venous thrombosis. For the analysis, scientific articles published between 1828 and 2020 were selected. Thirty percent of the analyzed works on the subject of CVT are not older than 5 years.

**CONCLUSION** Due to the various clinical manifestations and the absence of pathognomonic symptoms, neuroimaging plays a leading role in establishing the diagnosis. Early diagnosis of cerebral venous thrombosis and the use of anticoagulants lead to a decrease in disability and mortality.

**Keywords:** cerebral venous thrombosis, cryptogenic stroke, intracerebral hemorrhage, neuroimaging is not necessary for cerebral venous thrombosis, anticoagulant therapy

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**Affiliations**

| | |
|---|---|
| Ganipa R. Ramazanov | Candidate of Medical Sciences, Head of the Department of Emergency Neurology and Rehabilitation Treatment, N.V. Sklifosovsky Research Institute for Emergency Medicine;<br>https://orcid.org/0000-0001-6824-4114, ramazanovgr@sklif.mos.ru;<br>40%, preparation of the outline from the article, making corrections, editing |
| Khedi V. Korigova | Neurologist, Neurological Department for Patients with Acute Cerebrovascular Accidents, N.V. Sklifosovsky Research Institute for Emergency Medicine;<br>https://orcid.org/0000-0002-9788-592X, khadi.korigova@mail.ru;<br>30%, collecting primary material, writing the main text of the article, preparing the text for printing |
| Sergei S. Petrikov | Corresponding Member of the Russian Academy of Sciences, Doctor of Medical Sciences, Director of N.V. Sklifosovsky Research Institute for Emergency Medicine;<br>https: //orcid.org/0000-0003-3 292-8789, petrikovss@sklif.mos.ru;<br>30%, text editing, final approval of the text |

ICH – intracerebral hemorrhage
SSS – superior sagittal sinus
VTE – venous thrombotic events
ICH – intracranial hypertension

ICP – intracranial pressure
ICH – intracranial hemorrhage
HA – headache
GCS – glucocorticosteroids
DC – decompressive craniotomy
DSA – digital subtraction angiography
VD – visual disorders
IS – ischemic stroke
CS – cryptogenic stroke
CSi – cavenous sinus
CT – computed tomography
INR – international normalized ratio
MRI – Magnetic Resonance Imaging
LMWH – low molecular weight heparin
UFH – unfractionated heparin
OAC – oral anticoagulants
EONH – edema of the optic nerve head
ADCC – acute disorders of cerebral circulation
PG – pachyon granulation
TS – transverse sine
TGA – Transient Global Amnesia
PE – pulmonary embolism
CVT – cerebral venous thrombosis
GCS – Glasgow Coma Scale
ET – endovascular treatment
ES – epileptic seizures
SE – status epilepticus

## INTRODUCTION

Acute disorders of cerebral circulation (ADCC) is a heterogeneous syndrome with many etiological factors. In 20–40% of patients with ischemic stroke (IS), it is not possible to establish its cause. In this case, it is customary to talk about cryptogenic stroke (CS). It is very likely that among patients with CS there is a proportion of patients with cerebral venous thrombosis (CVT), in whom IS was erroneously diagnosed due to the similarity of clinical and radiological manifestations of these diseases. It should be noted that the treatment of patients and secondary prevention in patients with IS and CVT differ significantly [1-3].

Cerebral venous thrombosis (CVT), which is essentially one of the variants of ADCC, is a cerebrovascular disease that combines thrombosis of the dura mater sinuses and thrombosis of cerebral veins. This condition was first described in 1825 by Ribes M. in a 45-year-old patient with headache, convulsions and delirium. The diagnosis was confirmed by autopsy, which revealed thrombosis of the superior sagittal (SSS) and transverse sinuses (TS) [4]. In 1828, Abercrombie J. described for the first time a case of CVT in the postpartum period in a 24-year-old female patient. Autopsy in this case revealed thrombosis of SSS and superficial cerebral veins [5].

The incidence rate of CVT varies from 3 to 13 cases per 1,000,000 population per year [6–7]. A significant scatter of statistical indicators, most likely, is associated with the use of various diagnostic methods. According to Gunes H.N. et al. (2015), CVT in women is detected 5 times more often than in men [8]. The incidence rate of CVT in the perinatal period in women is 11.6 cases per 100,000 population per year [9]. In the overwhelming majority of cases (up to 78%), CVT is developed in patients under 50 years of age [10, 11]. According to the RENAMEVASC register, CVT was detected in 3% of stroke patients [12]. Janghorbani M. et al. (2008) found that in 5% of young patients, intracerebral hemorrhage (ICH ) was caused by CVT [13]. A postmortem examination of 182 patients showed a high detection rate of CVT - 9.3% [14]. Such a high rate, most likely, is due to the fact that CVT can be not only the direct cause of patients death, but also one of the terminal complications in patients with cardiovascular diseases.

Currently, three types of CVT are distinguished: 1) thrombosis of the venous sinuses of the dura mater, 2) thrombosis of the deep cerebral veins - thrombosis of the Galen vein, the basal vein of Rosenthal and their tributaries (direct sinus is recognized by most anatomists as a deep cerebral vein), 3) thrombosis of cortical cerebral veins, including the anastomotic vein of Labbe. The most common type of CVT is venous sinus thrombosis. Deep cerebral vein thrombosis is observed in 10% of patients with CVT [7, 10, 14, 15].

In most cases, thrombosis of several sinuses of the dura mater is detected. In a study by Sassy S.B. et al. (2017), 71.2% of patients were diagnosed with thrombosis of several sinuses [16]. According to Sidhom Y. et al. (2014) thrombosis PS (56%) and SCD (51%) most often was detected [17]. Thrombosis of the cavernous sinus (CSi) is the least commonly diagnosed - 1.3% of cases [15]. Frequent involvement in the SSS process is currently explained by the fact that superficial cortical veins flow into this sinus against the blood flow in it, which, along with the presence of fibrous septa inside the sinus, creates conditions for turbulent blood flow, and this, in turn, predisposes to its thrombosis [18].

According to Nasr D.M. et al. (2013), hospital mortality in CVT does not exceed 2% [19], while Krayenbuhl H.A. et al. reported about mortality rate of 38% in 1968 [20]. Such a significant difference is associated with the modern possibilities of intravital diagnosis of CVT, as well as the use of anticoagulant therapy. Hiltunen S. et al. (2016) observed a good outcome of the disease - 0–1 points on the modified Rankin scale, in 80% of patients with CVT [21]. The incidence of repeated CVT is 2-3%, and subsequent extracranial thrombotic events reaches 8% [22]. Thus, Ava L Liberman et al. (2017) found that the development of pulmonary embolism (PE) is observed in 1.4% of patients with CVT, and over the next 5 years - in 6.6% [23].

## PATHOPHYSIOLOGY OF CEREBRAL VENOUS THROMBOSIS

Currently, two main pathophysiological processes have been described that lead to the development of clinical and morphological manifestations of CVT. The first is that cerebral venous thrombosis leads to an increase in venous and capillary pressure and, as a consequence, to a decrease in cerebral perfusion. In turn, cerebral hypoperfusion leads to ischemic damage, which is manifested by cytotoxic edema and the blood-brain barrier damage, followed by the development of vasogenic edema. Increased pressure in the cerebral venous system can lead to intracerebral hemorrhage.

The second pathophysiological process that accompanies CVT is a violation of the absorption of cerebrospinal fluid into the venous sinuses due to their thrombosis, which leads to an increase in intracranial pressure (ICP), cytotoxic and vasogenic edema with the subsequent possible development of intracranial hemorrhage [24]. Adequacy of collateral venous drainage determines the symptoms of the disease. In the case when venous drainage is sufficient, symptoms of intracranial hypertension (ICH) develop, and in the case of collateral failure, a venous infarction with hemorrhagic transformation and corresponding clinical manifestations is formed [25].

## CLINICAL MANIFESTATIONS

The absence of clinical symptoms pathognomonic for CVT, as well as unified neuroimaging protocols, cause difficulties in the intravital diagnosis of CVT. The clinical manifestations of CVT are variable and depend on the localization of thrombosis and the rate of its development. An equally important component of the clinical picture of CVT is the underlying disease. It has been established that CVT can be a complication of oncological diseases, as well as a terminal manifestation in patients with congestive heart failure [14].

Focal neurological symptoms and epileptic seizures (ES) at the onset of the disease are observed in 37.2 and 39.3% of patients, respectively [15]. According to Ferro et al. (2009), 80% of patients with CVT have an acute or subacute onset, and 20% of patients are admitted to the hospital in the chronic stage of the disease (at least 13 days). Due to the absence of specific clinical manifestations and subacute onset, the average period from the onset of the disease to the diagnosis is 7 days [26]. A decrease in the level of wakefulness and ES upon admission of a patient to the hospital lead to an acceleration of diagnosis [26]. It should be noted that approximately in 0.1% of cases, CVT may manifest as symptoms of a transient ischemic attack [10, 15, 27-29].

The most common symptom of CVT is headache (HA) of varying intensity, which affects 80–90% of patients [15, 26, 30]. In most cases, HA in patients with CVT is accompanied by focal neurological deficits, a decrease in the level of wakefulness or ES. However, in 14–40% of patients, hypertension may be the only symptom of CVT [31, 32]. Saposnik G. et al. (2011) pointed out such characteristics of HA in patients with

CVT, as its intensification in the supine position, as well as against the background of taking Valsalva [33]. Botta R. et al. (2017) revealed the following patterns of HA in patients with CVT: the average duration of HA was 12.6 ± 26.8 days, the intensity of HA according to the visual analogue scale was 79.38 ± 13.41 points [34]. HA was acute in 51.1%, patients with subacute - in 42.6%, the "thunderclap" type - in 4.3% and chronic - in 2.1%. The most frequent localization of HA is the holocranial (36.2%) and frontal areas (27.7%). In the vast majority of cases, HA was pulsating (44.7%) or aching (25.5%). There was no connection between HA lateralization and the side of the thrombosed sinus [34]. In a study by Wasay M. et al. (2010) in 61% of patients with sigmoid thrombosis (SS) and / or TS at the onset of the disease, pain in the cervical or occipital region was observed [35]. One should take into account the fact that HA may be the only manifestation of CVT, and its characteristics may correspond to migraine-like or cluster HA, which complicates the diagnosis of CVT [36].

Epileptic seizures at the onset of CVT are observed in 39.3–46% of patients [37–39]. ES in CVT can be both single and repetitive. Status epilepticus (SE) is detected in 5.6–7% of patients with CVT [37, 39]. In a study by Masuhr F. et al. (2006) was found that in patients with CVT and SE, mortality was 3 times higher than in patients without SE (36.4% versus 12%, respectively) [37]. In more recent studies, Kalita J. et al. (2012) and Mahale R. et al. (2016) these data were not confirmed [39, 40]. However, Masuhr F. et al. (2006) identified the following independent predictors of SE development in patients with CVT: motor deficit, cortical vein thrombosis and signs of intracranial hemorrhage (OR 5.8; 95% CI 2.98-11.42; p <0.001; OR 2.9; 95% CI 1.43-5.96; p = 0.003; OR 2.8; 95% CI 1.46-5.56; p = 0.002, respectively) [37]. In a study by Mahale R. et al. (2016) also was identified the risk factors for the development of ES in patients with CVT: a decrease in the level of wakefulness to 8 points on the Glasgow coma scale (GCS), motor deficit, hemorrhagic infarction according to computed tomography (CT) of the brain, SSS thrombosis and the presence of the damage focus to the frontal lobe [39]. Despite the fact that the present recommendations for the diagnosis and treatment of patients with CVT do not provide for the preventive administration of antiepileptic drugs, the above-described predictors of the development of ES can be considered as a guide to action [37, 39]. According to Uluduz D. et al. (2020), ES in the first 48 hours was detected in 23.9% of patients [41]. In 31.4% of cases, this symptom was combined with a decrease in the level of wakefulness and was associated with poor functional and clinical outcomes by the 30th day of the disease. Thrombosis of SSS and cortical cerebral veins have been identified as independent prognostic factors for the ES development [41].

Focal neurological deficit, like other clinical symptoms in patients with CVT, is not a pathognomonic manifestation of this disease. Most often, movement disorders are observed - 19.1–39% [10, 15, 27–29]. It was found that focal neurological symptoms are more typical for CVT of non-infectious etiology [42]. According to Ferro J.M. et al. (2004) and Sparaco M. et al. (2015), speech disorders in the form of aphasia were detected in 19% and 24% of patients with CVT, respectively [15, 43]. Aphasia was more often observed in patients with thrombosis of the left TS or deep cerebral veins [10]. Focal symptoms such as diplopia, sensory disturbances and cortical blindness are observed in 13.5%, 5.4% and 13.2% of patients, respectively [15]. According to Ameri A. et al. (1992), 12% of patients with CVT showed symptoms of cranial nerve damage [44].

Visual disturbances (VD) in the form of the concentric constriction of the visual fields, homonymous hemianopsia, or cortical blindness are detected in 8.7–23% of patients with CVT [15, 35, 45]. Increased ICP, the formation of foci of cerebral infarction, or parenchymal hemorrhages in the occipital lobe are the main causes of VD in patients with CVT [46]. VD due to increased ICP are developed gradually, while an acute decrease in vision in the form of cortical blindness or homonymous hemianopsia is most typical for patients with foci in the occipital lobe [46]. Long-term ICH, manifested by edema of the optic nerve head (EONH), can lead to atrophy of the optic nerve and, as a consequence, to a decrease in visual acuity, which in most cases is irreversible [47, 48]. Despite the fact that ophthalmoscopy is not the basic method for diagnosing CVT, the EONH, which can be detected in this study, can help in establishing the diagnosis. EONH is a fairly common symptom that is diagnosed in 28–67.5% of patients with CVT. The absence of HA with a high degree of probability excludes the presence of this symptom in a patient with CVT [15, 35, 45, 49, 50]. According to Coutinho J. M. et al. (2014), EONH was more often detected in patients with cortical hemorrhage compared with those patients who did not have these radiological changes (44% versus 9%) [49]. It should also be noted that in patients with acute onset of the disease, EONH is detected less frequently than in patients with subacute onset and in the chronic stage (15% versus 32% and 44%, respectively) [51].

A decrease in the level of wakefulness is detected in 26–30.6% of patients with CVT [15, 16, 28, 29]. So, Sassi S.B. et al. (2017) in 23.2% of patients with CVT at the onset of the disease, a decrease in the level of wakefulness from superficial stunning to stupor (from 14 to 8 points on the GCS) was observed, and in 2.1% of patients - from moderate to atonic coma (from 7 to 3 points on GCS) [16]. A decrease in the level of wakefulness is more often observed in patients with deep brain vein thrombosis , compared with thrombosis of superficial cerebral veins (61.5% versus 17.1%, respectively) [52]. The most common radiological manifestation in patients with deep cerebral vein thrombosis, according to Pfefferkorn T. et al. (2009), there was edema in the thalamus (69%), which was bilateral in 47% of patients [53]. Despite the fact that a decrease in the level of wakefulness at the onset of CVT accelerates the diagnosis of the disease, in 41% of patients this symptom is associated with poor functional and clinical outcomes of the disease [54].

Idiopathic ICH (also known as pseudotumor cerebri) is a syndrome of increased ICP without apparent reason. [55]. Symptoms include headache, nausea, vomiting, signs of cranial nerve dysfunction, visual disturbances, and EONH. CVT can be both a cause and a consequence of ICH syndrome and should be excluded in all patients with these manifestations [56].

Despite the fact that such neurological symptoms as ataxia, nausea and vomiting occur in CVT no more often than in 27.8% of patients, their presence may indicate the formation of parenchymal lesions in the cerebellar region [41]. According to Ferro J.M. et al. (2004) and Kulkarni G.B. et al. (2014), in 0.3–1.8% of patients with CVT lesions are developed in the cerebellar region, and mortality in this group reaches 33% [15, 57].

Currently, there are few reports of CVT that debuted with psychiatric symptoms such as abulia and time disorientation [58, 59]. CVT can debut with symptoms of transient global amnesia (TGA). So, Sharma R.C. et al. (2015) described a clinical case of TGA in a 58-year-old man with SSS thrombosis [60]. Isolated pulsating noise in the ear has been described by Pons Y. et al. (2012) in a patient with sigmoid sinus thrombosis [61].

## NEUROVISUALIZATION

Neuroimaging is crucial in the diagnosis of CVT. Currently, CT, magnetic resonance imaging (MRI) and digital subtraction angiography (DSA) are used to diagnose this disease. Radiological signs of CVT detected by CT and MRI can be conditionally divided into direct (direct visualization of thrombosis) and indirect. Identification of the former is the basis of diagnosis, since indirect signs in the form of parenchymal changes with the formation of foci of subacute ischemia, ischemia with hemorrhagic transformation, or signs of intracranial hemorrhage (ICH) are not pathognomonic changes for CVT. It should be taken into account that parenchymal changes may be absent in more than 25% of patients [10]. The main task of CT in patients with suspected CVT is to exclude other pathology, for example, a brain tumor [62].

Despite the fact that CT of the brain without contrast enhancement in most patients does not reveal direct signs of cerebral vein thrombosis, there may be indirect signs that allow one to suspect CVT. Ischemic changes that do not fit into the arterial pool of blood supply, or are in the immediate vicinity of the venous sinus, may suggest CVT [63]. In 30–40% of patients with CVT, radiological signs of ICH are detected [28, 64]. Coutinho J. M. et al. (2014) found that juxtacortical foci of hemorrhage (less than 20 mm in diameter, localized in the white matter directly under the cerebral cortex) are a characteristic CT-pattern for CVT. Thus, out of 53 patients with ICH against a background of CVT, in 14 (26%) juxtacortical foci of hemorrhage were visualized according to CT data. This radiological pattern was observed only in 1.5% of patients with ICH of another nontraumatic etiology [65]. Subarachnoid hemorrhages in patients with CVT are detected in 0.5–0.8% of patients [15, 28, 66], and their isolated convexital localization is more typical for CVT than for hemorrhages against the background of ruptured aneurysms [33].

Erosion of the structures of the middle ear and changes in X-ray density from the cells of the mastoid process can serve as an indirect sign of thrombosis of the TS or sigmoid sinuses of septic etiology [62, 67]. Venous infarctions with or without hemorrhagic saturation are detected in 45% of patients with CVT. CVT may be favored by multifocality, inconsistency of the infarction zone with the arterial pool of blood supply, subcortical localization and bilateral involvement of the thalamus and / or basal ganglia [6, 68]. Hypodense changes around the hemorrhage zone in patients with CVT are characterized by their eccentricity, while intracerebral hemorrhages not associated with CVT are characterized by the formation of a symmetric hypodense surrounding area of edema [62].

Computed tomography without contrast enhancement has a low sensitivity in relation to the detection of CVT (25–56%), but in the case of the direct signs detection - high specificity [69–71]. An increase in X-ray density (hyperdensity) of cerebral veins and sinuses on CT without contrast enhancement is a direct sign of CVT. These include the "cord" symptom and the "triangle" symptom, which may indicate thrombosis of superficial (less often deep) cerebral veins and SSS thrombosis, respectively. According to Guenther G. et al. (2012), "cord" and "triangle" symptoms were detected in 25% and 60% of patients with CVT, respectively [25]. Lateral and transverse sinuses in the case of their thrombosis can also be hyperdense for CT without contrast enhancement [72]. It should be borne in mind that an increase in the X-ray density of the sinuses or cerebral veins may be associated with polycythemia, high hemoglobin concentration, increased hematocrit, dehydration, which can lead to false positive diagnostics [73]. The cause of a false-positive CT scan without contrast enhancement may be a thickening of the sinus wall. For the purpose of differential diagnosis in the presence of a hyperdense sinus and / or vein, in order to avoid a false-positive result, it is necessary to measure the X-ray density of the disputed area. X-ray density over 64 HU is a fairly reliable criterion for CVT (sensitivity 85%, specificity 87%) [74]. During the first two weeks, thrombosed sinuses may be hyperdense at native CT [75]. Thrombosis more than 14 days old may be isodense and not give rise to an increase in X-ray density at CT examination [76]. At present, a clinical case of hypodense thrombosis of the transverse sinus by native CT has been described [77].

Computed tomography with contrast enhancement reveals such a direct sign of CVT as a symptom of "empty delta" - thrombotic masses inside the sinus look hypodense against the background of hyperdense collateral veins of the sinus wall that have accumulated contrast. The frequency of this symptom detection in patients with CVT varies widely - from 25 to 75% [69, 72]. It should be taken into account that the symptom of an empty delta can be false-negative in the following cases: if the posterior part of the SSS is not thrombosed, in the case of an early anatomical division of the SSS into transverse sinuses, the presence of additional septa inside the sinus, and also if the study was performed in the first 5 days from the beginning diseases [72]. In addition to direct signs of CVT, CT with contrast enhancement allows visualization of such indirect signs as accumulation of contrast agent along the tentorial of the cerebellum (20%), as well as its giral accumulation (10–20%) [78, 79]. The simultaneous presence of "triangle" symptoms at native CT and "empty delta" on contrast-enhanced CT enhances the accuracy of CVT diagnostics.

CT venography can diagnose CVT, which manifests itself as a defect in the accumulation of cerebral veins and / or sinuses. In a study by Ozvath R. R. et al. (1997) was showed that CT venography is better than MR venography in visualizing the cerebral venous system, and the diagnostic value of these two modalities in identifying CVT is comparable [80].

Anatomical variability of the cerebral venous system, congenital hypoplasia or aplasia of the sinuses, and the presence of pachyon granulations (PG) create additional complications in the diagnosis of CVT, and may lead to a false-positive result when performing CT venography or MR venography [81]. Thus, in a study by Gokce E. et al. (2014) was found that right TS dominates in 25.1% of healthy subjects, both TS are equally developed in 60.2%, and left TS predominates in 12.2% [82]. PG are normally found in the SSS, TS, cavernous sinus, superior petrosal sinus, and straight sinus in decreasing order of frequency. PG, unlike thrombosis, is never hyperdense on native CT and is not hyperintense on T1- WI (weighted images) MRI [83–85]. In the absence of filling the venous sinus during CT or MR venography, it is necessary to exclude its hypoplasia.

The MRI picture of direct signs of venous thrombosis depends on the age of the process, and the signal characteristics depend on the presence of degradation products of thrombotic masses [81]. Thus, during the first 3–5 days, the thrombosed sinus is iso-intensive on T1-WI and hypointense on T2-WI and FLAIR, which is difficult to distinguish from a normally functioning cerebral venous system [10, 86]. Starting from the 2nd week, the thrombus already contains methemoglobin, which leads to an increase in the signal intensity on T1-WI, T2-WI and FLAIR [6, 85]. An increase in signal intensity on T1-WI must be differentiated with fat accumulation. According to Tokiguchi S. (1991), the frequency of fat detection in the cavernous sinus is 20%, in other cerebral sinuses one does not exceed 3% [87]. The main MR sign of CVT is a combination of changes in the MR signal from the cerebral vein with the simultaneous absence of the MR signal on venography [10]. The isolated use of the brain MRI is associated with a high rate of false positives results due to flow artifacts, especially in the T2-FLAIR mode. The use of cerebral MR venography alone is limited by the fact that this diagnostic method does not allow for differential diagnosis between venous sinus thrombosis and its

hypoplasia [33]. Several studies have shown high sensitivity of T2 * SW-weighted echo-planar T2 images for detecting CVT, especially cortical veins [88–90]. So, in a study by Idbaih A. et al. (2006), this scan mode revealed a change in the intensity of the MR signal (hypointense signal) from thrombosed cortical veins in the first 3 days from the onset of the disease better than T1SE, FLAIR, DWI and T2SE (98%, 79%, 14%, 3% and 0 %, respectively) [90].

In a study by Linn J. et al. (2010), the purpose of which was to compare the diagnostic capabilities of the brain MRI in the modes T2 gradient echo (T2GE), T1, FLAIR, DWI, proton weighted images, MR venography, with non-contrast cerebral CT and CT angiography in relation to the detection of cerebral sinuses thrombosis and cortical veins, T2GE was found to have the best ratio of sensitivity, specificity, interobserver agreement ratio, and positive and negative predictive values. The sensitivity and specificity of T2GE in detecting thrombosis of cortical veins and venous sinuses was (98.6%, 100% and 96.7%, 100%, respectively) [91].

Currently, the combination of brain MRI (T1SE, T2SE, FLAIR, T2 * SW, T2GE) and cerebral MR venography has led to the fact that digital subtraction angiography is required to confirm CVT only in exclusive cases [10]. The highest sensitivity and specificity for the detection of CVT were found in the three-dimensional T1 gradient echo with contrast enhancement (CE-3D-T1GE) (100% true positive results) [92].

Digital subtraction angiography should be a backup diagnostic or treatment method. Despite the fact that CT venography is a fairly reliable diagnostic tool for detecting CVT, a number of factors limit the use of this modality, namely, allergic reactions to contrast iodine contained in the drug, the impossibility of using it in patients with renal insufficiency, and an increase in dosimetric cost. Therefore, the use of MR venography is preferred. The limitations of digital subtraction angiography are similar to those in CT venography. Taking into account all of the above, the optimal method for verification of CVT is MRI in T1GE modes with contrast enhancement, T1, DWI, FLAIR, T2 and venography. Isolated venography is not recommended due to the anatomical variability of the brain cerebral venous system, sinus hypoplasia, and in some cases, the absence of one transverse sinus, which occurs in 20% of patients.

## TREATMENT

The basis of CVT therapy is the urgent prescription of anticoagulant therapy. The main tasks of using anticoagulants in patients with CVT are to prevent an increase in CVT and clinical deterioration, reduce mortality, accelerate thrombosis recanalization, and prevent any venous thrombotic events [33, 93]. Currently, low molecular weight (LMWH) and unfractionated heparin (UFH) are used effectively and safely in patients with CVT [93–97].

Thus, in the study by Einhaupl K.M. et al. (1991) it was found that against the background of intravenous use of UFH, the score on the CVT severity scale on days 3, 8, and 21 was significantly lower than in patients who received placebo (2.9 versus 3.8, $p < 0.05$; 1.5 versus 3.6, $p < 0.01$; 0.6 versus 3.9, $p < 0.005$, respectively). By the 90th day of the disease, complete recovery was observed in 80% of patients who received UFH, and only in 10% of patients in the placebo group. It was also found that intravenous use of UFH is safe and effective in patients with ICH associated with CVT. Mortality in the UFH group in patients with CVT and ICH was significantly lower than in the placebo group (15% versus 69%). Complete recovery of neurological functions was significantly more frequently observed in the intravenous UFH group compared with the placebo group (52% versus 23%) [95].

In a study by de Brujin S.F. et al. (1997) it was found that the subcutaneous use of LMWH nadroparin calcium by 180 units of anti-Xa factor per kilogram of body weight per day compared with placebo in patients with CVT was accompanied by a higher frequency of favorable clinical outcomes. By the end of the 12th week in the study group, the number of patients who achieved complete independence in daily life was 90% versus 79% in the placebo group, and the number of adverse outcomes (death or at least 3 points on the Oxford scale of outcomes) was 13% and 21% respectively.

Mortality by the end of the 2nd week in the main and comparison groups was 7% and 14%, respectively. The study did not show the development of new symptomatic cerebral bleeding. Anticoagulant therapy, as shown in this study, is safe even in patients with ICH associated with CVT [94].

In a study by Misra U.K. et al. (2012), whose purpose was to compare the effectiveness of the use of LMWH sodium dalteparin (100 U / kg / day subcutaneously) and UFH (80 U / kg / day intravenously) in patients with CVT, it was found that mortality with the use of LMWH is significantly lower than in the UFH group (0%

versus 18.8%, p <0.01) [96]. Complete recovery of neurological functions by the 90th day of the disease was more often observed in patients who received LMWH than in patients from the UFH group (88.2% versus 62.5%), and major hemorrhagic complications were more often diagnosed with the use of UFH than with the use of LMWH (9.4% versus 0%) [96].

Currently, the use of oral anticoagulants (OAC) in patients with CVT in the acute period is not recommended [33, 97]. The use of OAC is indicated for the secondary prevention of CVT and any veno-thrombotic events, however, a clear time frame for the initiation of this therapy has not been established. According to the American and European guidelines for the diagnosis and treatment of patients with CVT, secondary prophylaxis in patients with an established and treatable cause should be carried out with vitamin K antagonists with an international normalized ratio (INR) target value of 2 to 3, and the duration of anticoagulant therapy should be from 3 to 6 months. Patients with an unknown cause of CVT are shown anticoagulants for a period of 6 to 12 months using vitamin K antagonists with an INR target value of 2 to 3 [33, 97]. The RESPECT CVT study, which compared the safety and efficacy of dabigatran etexilate 150 mg twice daily with warfarin (INR targets value of 2 to 3) for the prevention of venous thrombotic events (VTE) in patients with CVT, found the same efficacy profile and the safety of these drugs [98]. Major bleedings, repeated VTE and the frequency of recanalization of CVT in the groups of dabigatran etexilate and warfarin were 1.7% versus 3.3%, 0% versus 0% and 60% versus 67.3%, respectively [98]. At present, patients are still being enrolled in the SECRET study, which aim is to compare the efficacy and safety of rivaroxaban and heparin (LMWH or UFH) in the acute period of CVT [99].

Despite the high efficiency of anticoagulant therapy, clinical deterioration is noted in 37% of patients with CVT [100]. The TO-ACT study, which aim is to compare the efficacy and safety of endovascular therapy (ET) and anticoagulant therapy in patients with CVT against the background of predictors of poor functional outcome (mental status disorder, coma, deep cerebral vein thrombosis or ICH), wasnot established the advantage of ET compared with standard treatment [101]. Thus, the number of favorable clinical outcomes (mRS 0–1 points), mortality and frequency of symptomatic ICH in the groups of standard and endovascular treatment were 68% versus 67%, 3% versus 12% and 9% versus 3%, respectively [101]. According to European recommendations, ET is not recommended for use in patients with CVT, while American recommendations indicate that this type of treatment should be considered in case of clinical deterioration, despite conducting the anticoagulant therapy [33, 97].

In patients with CVT, the use of acetazolamide, glucocorticosteroids (GCS) and therapeutic lumbar puncture for the treatment of ICH is not currently recommended [97]. However, American recommendations allow the use of acetazolamide in patients with ICH as an initial therapy for this condition, and in the case of VD increase (as a manifestation of ICH) - lumbar puncture, neurosurgical shunting, or optic nerve decompression [33]. The use of GCS in patients with CVT is justified only in the case of its development against the background of Behcet's disease or another disease that requires their appointment [33, 97, 102].

Edema with subsequent dislocation of the brain is the leading cause of death in patients with CVT. In such a case, decompression craniotomy (DC) can be a life-saving procedure. Currently, there are no randomized studies on DC in patients with CVT. However, in 2 systematic reviews [103, 104] and two nonrandomized studies [103, 105], the purpose of which was to compare DC with its absence, it was shown that mortality does not exceed 18.5%, mortality plus disability is 32.2%, severe disability was noted in 3.4%, and complete recovery - in 30.7% of patients after DC. Thus, according to the European and American guidelines for the diagnosis and treatment of cerebral venous thrombosis, DC is recommended for patients with CVT with parenchymal lesions and signs of brain involvement in order to prevent death [33, 97].

The benefits of prophylactic administration of antiepileptic drugs to patients with CVT have not yet been established [33, 97]. However, their appointment is possible in order to prevent recurrent ES in patients with supratentorial lesions and already happened ES [33, 97].

## CONCLUSION

Cerebral venous thrombosis is a life-threatening condition and a potential cause of severe disability. Given the variety of clinical manifestations and the absence of pathognomonic symptoms, neuroimaging plays a leading role in establishing the diagnosis.

Cerebral venous thrombosis should be suspected in the following cases: the onset of the disease with a headache, the absence of traditional risk factors for acute cerebrovascular accident (in patients with cryptogenic ischemic stroke), an ischemic focus with hemorrhagic transformation according to neuroimaging data, a discrepancy between the ischemic focus and the brain arterial vascular supply . The optimal method of neuroimaging in patients with central venous thrombosis is magnetic resonance imaging in T1GE mode with contrast enhancement. To avoid false-positive results, isolated MR venography in patients with central venous thrombosis is not recommended. When the diagnosis of central venous thrombosis is confirmed, treatment with unfractionated or low molecular weight heparin should be initiated as soon as possible, even in the presence of intracranial hemorrhage. Digital subtraction angiography should not currently be considered as a diagnostic procedure in a patient with suspected central venous thrombosis, but as an option for endovascular treatment in patients with predictors of poor outcome and clinical deterioration. The appointment of antiepileptic drugs should be considered in patients with an already existing epileptic seizure against the background of present central venous thrombosis in the presence of a supratentorial lesion. Decompressive trepanation is indicated for patients with central venous thrombosis with parenchymal lesions and signs of brain involvement in order to prevent death. The appointment of oral anticoagulants in the acute period of central venous thrombosis currently does not have a sufficient evidence base. Their appointment is possible only for the prevention of recurrent central venous thrombosis and any venous thrombotic events.

## REFERENCES


1. Glebov MV, Maksimova MYu, Domashenko MA, Bryukhov VV. Trombozy tserebral'nykh venoznykh sinusov. *Annals of Clinical and Experimental Neurology.* 2011;5(1):4–10 (in Russ.).
2. Maksimova MYu, Dubovitskaya YuI, Bryukhov VV, Krotenkova MV. Diagnosis of cerebral veins and venous sinuses thrombosis. *RMJ*. 2017;(21):1595–1601. (in Russ.)
3. Chukanova EI, Chukanova AS, Mamayeva KhI. Cerebral venous thrombosis. *S.S. Korsakov Journal of Neurology and Psychiatry*. 2016;116(10):4–10. https://doi.org/10.17116/jnevro20161161014-10
4. Daif A, Awada A, Al-Rajeh S, Abduljabbar M, Al Tahan AR, Obeid T, et al. Cerebral Venous Thrombosis in Adults. A Study of 40 Cases from Saudi Arabia. *Stroke*. 1995;26(7):1193–1195. PMID: 7604412 https://doi.org/10.1161/01.str.26.7.1193
5. Abercrombie J. *Pathological and Practical Researches on Diseases of the Brain and Spinal Cord.* Edinburgh: Waugh and Innes;1828.
6. Stam J. Thrombosis of the cerebral veins and sinuses. *N Engl J Med*. 2005;352(17):1791–1798. PMID: 15858188 https://doi.org/10.1056/NEJMra042354
7. Coutinho JM, Zuurbier SM, Aramideh M, Stam J. The incidence of cerebral venous thrombosis: a cross-sectional study. *Stroke*. 2012;43(12):3375–3377. PMID: 22996960 https://doi.org/10.1161/STROKEAHA.112.671453
8. Gunes HN, Cokal BG, Guler SK, Yoldas TK, Malkan UY, Demircan CS, et al. Clinical associations, biological risk factors and outcomes of cerebral venous sinus thrombosis. *J Int Med Res*. 2016;44(6):1454–1461. PMID: 28222615 https://doi.org/10.1177/0300060516664807
9. Lanska DJ, Kryscio RJ. Risk factors for peripartum and postpartum stroke and intracranial venous thrombosis. *Stroke*. 2000;31(6):1274–1282. PMID: 10835444 https://doi.org/10.1161/01.str.31.6.1274
10. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol*. 2007;6(2):162–170. PMID: 17239803 https://doi.org/10.1016/S1474-4422(07)70029-7
11. Canhão P, Ferro JM, Lindgren AG, Bousser MG, Stam J, Barinagarrementeria F; ISCVT Investigators. Causes and predictors of death in cerebral venous thrombosis. *Stroke*. 2005;36(8):1720–1725. PMID: 16002765 https://doi.org/10.1161/01.STR.0000173152.84438.1c
12. Ruiz-Sandoval JL, Chiquete E, Bañuelos-Becerra LJ, Torres-Anguiano C, González-Padilla Ch, Arauz A, et al. Cerebral venous thrombosis in a Mexican multicenter registry of acute cerebrovascular disease: the RENAMEVASC study. *J Stroke Cerebrovasc Dis.* 2012;21(5):395–400. PMID: 21367622 https://doi.org/10.1016/j.jstrokecerebrovasdis.2011.01.001
13. Janghorbani M, Zare M, Saadatnia M, Mousavi SA, Mojarrad M, Asgari E. Cerebral vein and dural sinus thrombosis in adults in Isfahan, Iran: frequency and seasonal variation. *Acta Neurol Scand*. 2008;117(2):117–121. PMID: 18184347 https://doi.org/10.1111/j.1600-0404.2007.00915.x
14. Towbin A. The syndrome of latent cerebral venous thrombosis: its frequency and relation to age and congestive heart failure. *Stroke*. 1973;4(3):419–430. PMID: 4713031 https://doi.org/10.1161/01.str.4.3.419
15. Ferro JM, Canhao P, Stam J, Bousser M-G, Barinagarrementeria F; ISCVT Investigators. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke*. 2004;35(3):664–670. PMID: 14976332 https://doi.org/ 10.1161/01.STR.0000117571.76197.26
16. Sassi SB, Touati N, Baccouche H, Drissi C, Romdhane NB, Hentati F. Cerebral Venous Thrombosis: A Tunisian Monocenter Study on 160 Patients. *Clin Appl Thromb Hemost*. 2017;23(8):1005–1009. PMID: 27582021 https://doi.org/10.1177/1076029616665168
17. Sidhom Y, Mansour M, Messelmani M, Derbali H, Fekih-Mrissa N, Zaouali J, et al. Cerebral venous thrombosis: clinical features, risk factors, and long-term outcome in a Tunisian cohort. *J Stroke Cerebrovasc Dis*. 2014;23(6):1291–1295. PMID: 24462460 https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.10.025
18. Prakash C, Bansal BC. Cerebral venous thrombosis. *J Indian Acad Clin Med.* 2000;5(1):55–61. Available at: http://medind.nic.in/jac/t00/i1/jact00i1p55.pdf [Accessed Jul 13, 2020].
19. Nasr DM, Brinjikji W, Cloft HJ, Saposnik G, Rabinstein AA. Mortality in cerebral venous thrombosis: results from the national inpatient sample database. *Cerebrovasc Dis*. 2013;35(1):40–44. PMID: 23428995 https://doi.org/10.1159/000343653
20. Krayenbuhl HA. Cerebral venous and sinus thrombosis. *Neurol Med Chir.* 1968;10:1–24. PMID: 4194573 https://doi.org/10.2176/nmc.10.1

21. Hiltunen S, Putaala J, Haapaniemi E, Tatlisumak T. Long-term outcome after cerebral venous thrombosis: analysis of functional and vocational outcome, residual symptoms, and adverse events in 161 patients. *J Neurol*. 2016;263(3):477–484. PMID: 26725090 https://doi.org/10.1007/s00415-015-7996-9
22. Palazzo P, Agius P, Ingrand P, Ciron J, Lamy M, Berthomet A, et al. Venous Thrombotic Recurrence After Cerebral Venous Thrombosis A Long-Term Follow-Up Study. *Stroke*. 2017;48(2):321–326. PMID: 27980127 https://doi.org/10.1161/STROKEAHA.116.015294
23. Liberman AL, Merkler AE, Gialdini G, Messé SR, Lerario MP, Murthy SB, et al. Risk of Pulmonary Embolism after Cerebral Venous Thrombosis. *Stroke*. 2017;48(3):563–567. PMID: 28228575 https://doi.org/10.1161/STROKEAHA.116.016316
24. Piazza G. Cerebral Venous Thrombosis. *Circulation*. 2012;125(13):1704–1709. PMID: 22474313 https://doi.org/10.1161/CIRCULATIONAHA.111.067835
25. Guenther G, Arauz A. Cerebral venous thrombosis: A diagnostic and treatment update. *Neurología*. 2011;26(8):488–498. PMID: 21163216 https://doi.org/10.1016/j.nrl.2010.09.013
26. Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F, Massaro A, et al. Delay in the diagnosis of cerebral vein and dural sinus thrombosis: influence on outcome. *Stroke*. 2009;40(9):3133–3138. PMID: 19608994 https://doi.org/10.1161/STROKEAHA.109.553891
27. Paciaroni M, Palmerini F, Bogousslavsky J. Clinical presentations of cerebral vein and sinus thrombosis. *Front Neurol Neurosci*. 2008;23:77–88. PMID: 18004054 https://doi.org/10.1159/000111262
28. Wasay M, Bakshi R, Bobustuc G, Kojan S, Sheikh Z, Dai A, et al. Cerebral venous thrombosis: analysis of a multicenter cohort from the United States. *J Stroke Cerebrovasc Dis*. 2008;17(2):49–54. PMID: 18346644 https://doi.org/10.1016/j.jstrokecerebrovasdis.2007.10.001
29. Uzar E, Ekici F, Acar A, Yucel Y, Bakir S, Tekbas G, et al. Cerebral venous sinus thrombosis: an analyses of 47 patients. *Eur Rev Med Pharmacol Sci*. 2012;16(11):1499–1505. PMID: 23111961
30. Agostoni E. Headache in cerebral venous thrombosis. *Neurol Sci*. 2004;25(Suppl 3):S206–210. PMID: 15549538 https://doi.org/10.1007/s10072-004-0287-3
31. Cumurciuc R, Crassard I, Sarov M, Valade D, Bousser MG. Headache as the only neurological sign of cerebral venous thrombosis: a series of 17 cases. *J Neurol Neurosurg Psychiatry*. 2005;76(8):1084–1087. PMID: 16024884 https://doi.org/10.1136/jnnp.2004.056275
32. Timóteo Â, Inácio N, Machado S, Pinto AA, Parreira E. Headache as the sole presentation of cerebral venous thrombosis: a prospective study. *J Headache Pain*. 2012;13(6):487–490. PMID: 22592865 https://doi.org/10.1007/s10194-012-0456-3
33. Saposnik G, Barinagarrementeria F, Brown RD Jr, Bushnell CD, Cucchiara B, Cushman M, et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2011;42(4):1158–1192. PMID: 21293023 https://doi.org/10.1161/STR.0b013e31820a8364
34. Botta R, Donirpathi S, Yadav R, Kulkarni GB, Veerendra M K, Nagaraja D. Headache Patterns in Cerebral Venous Sinus Thrombosis. *J Neurosci Rural Pract*. 2017;8(Suppl 1):S72–S77. PMID: 28936075 https://doi.org/10.4103/jnrp.jnrp_339_16
35. Wasay M, Kojan S, Dai AI, Bobustuc G, Sheikh Z. Headache in Cerebral Venous Thrombosis: incidence, pattern and location in 200 consecutive patients. *J Headache Pain*. 2010;11(2):137–139. PMID: 20112042 https://doi.org/10.1007/s10194-010-0186-3
36. Luo Y, Tian X, Wang X. Diagnosis and Treatment of Cerebral Venous Thrombosis: A Review. *Front Aging Neurosci*. 2018;10:2. PMID: 29441008 https://doi.org/10.3389/fnagi.2018.00002
37. Masuhr F, Busch M, Amberger N, Ortwein H, Weih M, Neumann K, et al. Risk and predictors of early epileptic seizures in acute cerebral venous and sinus thrombosis. *Eur J Neurol*. 2006;13(8):852–856. PMID: 16879295 https://doi.org/10.1111/j.1468-1331.2006.01371.x
38. Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F; ISCVT Investigators. Early seizures in cerebral vein and dural sinus thrombosis: risk factors and role of antiepileptics. *Stroke*. 2008;39(4):1152–1158. PMID: 18309177 https://doi.org/10.1161/STROKEAHA.107.487363
39. Mahale R, Mehta A, John AA, Buddaraju K, Shankar AK, Javali M, et al. Acute seizures in cerebral venous sinus thrombosis: what predicts it? *Epilepsy Res*. 2016;123:1–5. PMID: 27023399 https://doi.org/10.1016/j.eplepsyres.2016.01.011
40. Kalita J, Chandra S, Misra UK. Significance of seizure in cerebral venous sinus thrombosis. *Seizure*. 2012;21(8):639–642. PMID: 22840965 https://doi.org/10.1016/j.seizure.2012.07.005
41. Uluduz D, Midi I, Duman T. Epileptic seizures in cerebral venous sinus thrombosis: Subgroup analysis of VENOST study. *Seizure*. 2020;78:113–117. PMID: 32353818 https://doi.org/10.1016/j.seizure.2020.02.017
42. Korathanakhun P, Petpichetchian W, Sathirapanya P, Geater SL. Cerebral venous thrombosis: comparing characteristics of infective and non-infective aetiologies: a 12-year retrospective study. *Postgrad Med J*. 2015;91(1082):670–674. PMID: 26499451 https://doi.org/10.1136/postgradmedj-2015-133592
43. Sparaco M, Feleppa M, Bigal ME. Cerebral Venous Thrombosis and Headache. A Case-Series. *Headache*. 2015;55(6):806–814. PMID: 26084237 https://doi.org/10.1111/head.12599
44. Ameri A, Bousser MG. Cerebral venous thrombosis. *Neurol Clin*. 1992;10(1):87–111. PMID: 1557011
45. Thammishetti V, Dharanipragada S, Basu D, Ananthakrishnan R, Surendiran D. A Prospective Study of the Clinical Profile, Outcome and Evaluation of D-dimer in Cerebral Venous Thrombosis. *J Clin Diagn Res*. 2016;10(6):OC07–10. PMID: 27504325 https://doi.org/10.7860/JCDR/2016/19114.7926
46. Das A, Huxlin KR. New approaches to visual rehabilitation for cortical blindness: outcomes and putative mechanisms. *Neuroscientist*. 2010;16(4):374–387. PMID: 20103505 https://doi.org/10.1177/1073858409356112
47. Messouak O, Alaoui Faris M, Benabdejlil M, Tizniti S, Belahsen F. Cerebral venous thrombosis secondary to essential thrombocythemia. *Rev Neurol (Paris)*. 2007;163(5):596–598. PMID: 17571029 https://doi.org/10.1016/s0035-3787(07)90467-1
48. O'Connor L, Croxson G, McCluskey P, Halmagyi GM. A 43-year-old woman presenting with subacute, bilateral, sequential facial nerve palsies, then developing pseudotumour cerebri. *BMJ Case Rep*. 2015;2015:bcr2015211399. PMID: 26604227 https://doi.org/10.1136/bcr-2015-211399
49. Coutinho JM, Gerritsma JJ, Zuurbier SM, Stam J. Isolated cortical vein thrombosis: systematic review of case reports and case series. *Stroke*. 2014;45(6):1836–1838. PMID: 24743438 https://doi.org/ 10.1161/STROKEAHA.113.004414
50. O'Rourke TL, Slagle WS, Elkins M, Eckermann D, Musick A. Papilloedema associated with dural venous sinus thrombosis. *Clin Exp Optom*. 2014;97(2):133–139. PMID: 23865959 https://doi.org/10.1111/cxo.12092
51. Ferro JM, Lopes MG, Rosas MJ, Fontes J, VENOPORT Investigators. Delay in hospital admission of patients with cerebral vein and dural sinus thrombosis. *Cerebrovasc Dis*. 2005;19(3):152–156. PMID: 15644627 https://doi.org/10.1159/000083248

52. Terazzi E, Mittino D, Rudà R, Cerrato P, Monaco F, Sciolla R, et al. Cerebral venous thrombosis: a retrospective multicentre study of 48 patients. *Neurol Sci*. 2005;25(6):311–315. PMID: 15729493 https://doi.org/10.1007/s10072-004-0363-8
53. Pfefferkorn T, Crassard I, Linn J, Dichgans M, Boukobza M, Bousser MG. Clinical features, course and outcome in deep cerebral venous system thrombosis: an analysis of 32 cases. *J Neurol*. 2009;256(11):1839–1845. PMID: 19536581 https://doi.org/10.1007/s00415-009-5206-3
54. Kowoll CM, Kaminski J, Weiß V, Bösel J, Dietrich W, Jüttler E, et al. Severe Cerebral Venous and Sinus Thrombosis: Clinical Course, Imaging Correlates, and Prognosis. *Neurocrit Care*. 2016;25(3):392–399. PMID: 27000641 https://doi.org/10.1007/s12028-016-0256-8
55. Krylov VV, Petrikov SS, Solodov AA. *Vnutricherepnaya gipertenziya*. Moscow: Binom Publ.; 2016. (in Russ.)
56. Leach JL, Fortuna RB, Jones BV, Gaskill-Shipley MF. Imaging of Cerebral Venous Thrombosis: Current Techniques, Spectrum of Findings, and Diagnostic Pitfalls. *RadioGraphics*. 2006;26(Suppl 1):S19–S43. PMID: 17050515 https://doi.org/ 10.1148/rg.26si055174
57. Kulkarni GB, Mustare V, Abbas MM. Profile of patients with cerebral venous sinus thrombosis with cerebellar involvement. *J Stroke Cerebrovasc Dis.* 2014;23(5):1106–1111. PMID: 24231137 https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.09.022
58. Hassan KM, Kumar D. Reversible diencephalic dysfunction as presentation of deep cerebral venous thrombosis due to hyperhomocysteinemia and protein S deficiency: Documentation of a case. *J Neurosci Rural Pract*. 2013;4(2):193–196. PMID: 23914104 https://doi.org/10.4103/0976-3147.112767
59. Xue SF, Ma QF, Ma X, Jia JP. Isolated cortical vein thrombosis: a widely variable clinicoradiological spectrum. *Eur Neurol*. 2013;69(6):331–335. PMID: 23549196 https://doi.org/10.1159/000346813
60. Sharma RC, Kainth A, Sharma S. Transient Global Amnesia as a Presenting Manifestation of Cerebral Venous Thrombosis. *J Neuropsychiatry Clin Neurosci.* 2015;27(3):e209–210. PMID: 26222971 https://doi.org/10.1176/appi.neuropsych.14110354
61. Pons Y, Vérillaud B, Ukkola-Pons E, Sauvaget E, Kania R, Herman P. Pulsatile tinnitus and venous cerebral thrombosis: report of a case and literature review. *Rev Laryngol Otol Rhinol (Bord)*. 2012;133(3):163–164. PMID: 23590107
62. Caso V, Agnelli G, Paciaroni M (eds). *Handbook on Cerebral Venous Thrombosis. Front Neurol Neurosci.* Basel: Karger; 2008. vol 23. pp 96–111.
63. Ford K, Sarwar M. Computed tomography of dural sinus thrombosis. *AJNR Am J Neuroradiol*. 1981;2(6):539–543. PMID: 6797278
64. Girot M, Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F, et al. Predictors of outcome in patients with cerebral venous thrombosis and intracerebral hemorrhage. *Stroke*. 2007;38(2):337–342. PMID: 17204682 https://doi.org/10.1161/01.STR.0000254579.16319.35
65. Coutinho JM, van den Berg R, Zuurbier SM, VanBavel E, Troost D, Majoie CB, et al. Small Juxtacortical Hemorrhages in Cerebral Venous Thrombosis. *Ann Neurol*. 2014;75(6):908–916. PMID: 24816819 https://doi.org/10.1002/ana.24180
66. Oppenheim C, Domigo V, Gauvrit JY, Lamy C, Mackowiak-Cordoliani MA, Pruvo JP, et al. Subarachnoid hemorrhage as the initial presentation of dural sinus thrombosis. *AJNR Am J Neuroradiol*. 2005;26(3):614–617. PMID: 15760875
67. Levine HR, Ha KY, O'Rourke B, Owens FD, Doughty KE, Opatowsky MJ. A pictorial review of complications of acute coalescent mastoiditis. *Proc (Bayl Univ Med Cent)*. 2012;25(4):372–373. PMID: 23077392 https://doi.org/10.1080/08998280.2012.11928882
68. Rao KCVG, Knipp HC, Wajner EJ. CT findings in cerebral sinus and venous thrombosis. *Radiology*. 1981;140(2):391–398. PMID: 7255715 https://doi.org/10.1148/radiology.140.2.7255715
69. Virapongse C, Cazenave C, Quisling R, Sarwar M, Hunter S. The empty delta sign: frequency and significance in 76 cases of dural sinus thrombosis. *Radiology*. 1987;162(3):779–785. PMID: 3809494 https://doi.org/10.1148/radiology.162.3.3809494
70. Vijay RK. The cord sign. *Radiology*. 2006;240(1):299–300. PMID: 16793988 https://doi.org/10.1148/radiol.2401031739
71. Teasdale E. Cerebral venous thrombosis: making the most of imaging. *J R Soc Med*. 2000;93(5):234–237. PMID: 10884765 https://doi.org/10.1177/014107680009300505
72. Masuhr F, Mehraein S, Einhäupl K. Cerebral venous and sinus thrombosis. *J Neurol*. 2004;251(1):11–23. PMID: 14999484 https://doi.org/10.1007/s00415-004-0321-7
73. Provenzale JM, Joseph GJ, Barboriak DP. Dural sinus thrombosis: findings on CT and MR imaging and diagnostic pitfalls. *AJR Am J Roentgenol*. 1998;170(3):777–783. PMID: 9490973 https://doi.org/10.2214/ajr.170.3.9490973
74. Avsenik J, Oblak JP, Popovic KS. Non-contrast computed tomography in the diagnosis of cerebral venous sinus thrombosis. *Radiol Oncol*. 2016;50(3):263–268. PMID: 27679541 https://doi.org/ 10.1515/raon-2016-0026
75. Haage P, Krings T, Schmitz-Rode T. Nontraumatic vascular emergencies: imaging and intervention in acute venous occlusion. *Eur Radiol*. 2002;12(11):2627–2643. PMID: 12386751 https://doi.org/10.1007/s00330-002-1615-8
76. Buyck P, De Keyzer F, Vanneste D,Wilms G, Thijs V, Demaerel P. CT density measurement and H:H ratio are useful in diagnosing acute cerebral venous sinus thrombosis. *Am J Neuroradiol*. 2013;34(8):1568–1572. PMID: 23471024 https://doi.org/10.3174/ajnr.A3469
77. Neal E, Sturgeon J. Hypodense cerebral venous sinus thrombosis on unenhanced CT: A potential pitfall. Report of a case and review of the literature. *Radiol Case Rep*. 2020;15(1):35–38. PMID: 31737143 https://doi.org/10.1016/j.radcr.2019.10.012
78. Einhäupl KM, Masuhr F. Cerebral venous and sinus thrombosis – an update. *Eur J Neurol*. 1994;1(2):109–126. PMID: 24283479 https://doi.org/10.1111/j.1468-1331.1994.tb00059.x
79. Bousser MG. Cerebral Venous Thrombosis. Nothing, Heparin, or Local Thrombolysis? *Stroke*. 1999;30(3):481–483. PMID: 10066839 https://doi.org/10.1161/01.str.30.3.481
80. Ozsvath RR, Casey SO, Lustrin ES, Alberico RA, Hassankhani A, Patel M. Cerebral Venography: Comparison of CT and MR Projection Venography. *AJR Am J Roentgenol*. 1997;169(6):1699–1707. PMID: 9393193 https://doi.org/ 10.2214/ajr.169.6.9393193
81. Alvis-Miranda HH, Castellar-Leones SM, Alcala-Cerra G, Moscote-Salazar LR. Cerebral sinus venous thrombosis. *J Neurosci Rural Pract*. 2013;4(4):427–438.
82. Gokce E, Pınarbas T, Acu B, Fırat MM, Erkorkmaz U. Torcular Herophili classification and evaluation of dural venous sinus variations using digital subtraction angiography and magnetic resonance venographies. *Surg Radiol Anat*. 2014;36(6):527–536. PMID: 24154635 https://doi.org/10.1007/s00276-013-1223-0
83. Choi HJ, Cho CW, Kim YS, Cha JH. Giant Arachnoid Granulation Misdiagnosed as Transverse Sinus Thrombosis. *J Korean Neurosurg Soc*. 2008;43(1):48–50. PMID: 19096547 https://doi.org/10.3340/jkns.2008.43.1.48
84. Tokiguchi S, Hayashi S, Takahashi H, Okamoto K, Ito J. CT of the pacchionian body. *Neuroradiology*. 1993;35(5):347–348. PMID: 8327108 https://doi.org/10.1007/BF00588366

85. Leach JL, Jones BV, Tomsick TA, Stewart CA, Balko MG. Normal appearance of arachnoid granulations on contrast-enhanced CT and MR of the brain: differentiation from dural sinus disease. *AJNR Am J Neuroradiol*. 1996;17(8):1523–1532. PMID: 8883652
86. Wasay M, Azeemuddin M. Neuroimaging of cerebral venous thrombosis. *J Neuroimaging*. 2005;15(2):118–128. PMID: 15746223 https://doi.org/10.1177/1051228404272883
87. Tokiguchi S. Investigation of fat in the dural sinus. *Nihon Igaku Hoshasen Gakkai Zasshi*. 1991;51(8):871–882. PMID: 1945768
88. Selim M, Fink J, Linfante I, Kumar S, Schlaug G, Caplan LR. Diagnosis of cerebral venous thrombosis with echo-planar T2*SW-weighted magnetic resonance imaging. *Arch Neurol*. 2002;59(6):1021–1026. PMID: 12056941 https://doi.org/10.1001/archneur.59.6.1021
89. Cakmak S, Hermier M, Montavont A, Derex L, Mauguière F, Trouillas P, et al. T2*SW-weighted MRI in cortical venous thrombosis. *Neurology*. 2004;63(9):1698. PMID: 15534258 https://doi.org/10.1212/01.wnl.0000138502.59539.cb
90. Idbaih A, Boukobza M, Crassard I, Porcher R, Bousser MG, Chabriat H. MRI of clot in cerebral venous thrombosis high diagnostic value of susceptibility-weighted images. *Stroke*. 2006;37(4):991–995. PMID: 16484607 https://doi.org/ 10.1161/01.STR.0000206282.85610.ae
91. Linn J, Michl S, Bochmann K, Pfefferkorn T, Wiesmann M, Hartz S, et al. Cortical vein thrombosis: the diagnostic value of different imaging modalities. *Neuroradiology*. 2010;52(10):899–911. PMID: 20107776 https://doi.org/10.1007/s00234-010-0654-0
92. Patel D, Machnowska M, Symons S, Yeung R, Fox AJ, Aviv RI, et al. Diagnostic performance of routine brain MRI sequences for dural sinus thrombosis. *Am J Neuroradiol.* 2016;37(11):2026–2032. PMID: 27313130 https://doi.org/10.3174/ajnr.A4843
93. Coutinho J, de Bruijn SFTM, deVeber G, Stam J. Anticoagulation for cerebral venous sinus thrombosis. *Stroke*. 2012;43(4):e41–e42. PMID: 22567669 https://doi.org/ 10.1161/strokeaha.111.648162
94. de Bruijn SF, Stam J. Randomized, placebo-controlled trial of anticoagulant treatment with low-molecularweight heparin for cerebral sinus thrombosis. *Stroke*. 1999;30(3):484–488. PMID: 10066840 https://doi.org/10.1161/01.str.30.3.484
95. Einhaupl KM, Villringer A, Meister W, Mehraein S, Garner C, Pellkofer M, et al. Heparin treatment in sinus venous thrombosis. *Lancet*. 1991;338:597–600. PMID: 1679154 https://doi.org/10.1016/0140-6736(91)90607-q
96. Misra UK, Kalita J, Chandra S, Kumar B, Bansal V. Low molecular weight heparin versus unfractionated heparin in cerebral venous sinus thrombosis: a randomized controlled trial. *Eur J Neurol*. 2012;19(7):1030–1036. PMID: 22416902 https://doi.org/10.1111/j.1468-1331.2012.03690.x
97. Ferro JM, Bousserc MG, Canhao P, Coutinhod JM, Crassardc I, Dentalie F, et al. European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – endorsed by the European Academy of Neurology. *Eur J Neurol*. 2017;24(10):1203–1213. PMID: 28833980 https://doi.org/10.1111/ene.13381
98. Ferro M., Coutinho M., Dentali F, Kobayashi A, Alasheev A, Canhão P, et al. Safety and Efficacy of Dabigatran Etexilate vs Dose-Adjusted Warfarin in Patients with Cerebral Venous Thrombosis. A Randomized Clinical Trial. *JAMA Neurol*. 2019;76(12):1457–1465. PMID: 31479105 https://doi.org/10.1001/jamaneurol.2019.2764
99. Study of Rivaroxaban for CeREbral Venous Thrombosis (SECRET). Available at: https://clinicaltrials.gov/ct2/show/NCT03178864 [Accessed Jul 13, 2020].
100. Yii IYL, Mitchell PJ, Dowling RJ, Yan B. Imaging Predictors of Clinical Deterioration in Cerebral Venous Thrombosis. *J Clin Neurosci*. 2012;19(11):1525–1529. PMID: 22796274 https://doi.org/10.1016/j.jocn.2012.02.005
101. Coutinho JM, Zuurbier SM, Bousser MG, Ji X, Canhão P, Roos YB, et al. Effect of Endovascular Treatment with Medical Management vs Standard Care on Severe Cerebral Venous Thrombosis: The TO-ACT Randomized Clinical Trial. *JAMA Neurol*. 2020 May 18;e201022. Online ahead of print. PMID: 32421159 https://doi.org/10.1001/jamaneurol.2020.1022
102. Hatemi G, Silman A, Bang D, Bodaghi B, Chamberlain AM, Gul A, et al. Management of Behcet disease: a systematic literature review for the European League Against Rheumatism evidence-based recommendations for the management of Behcet disease. *Ann Rheum Dis*. 2009; 68(10):1528–1534. PMID: 18420940 https://doi.org/10.1136/ard.2008.087957
103. Ferro JM, Crassard I, Coutinho JM, Canhão P, Barinagarrementeria F, Cucchiara B, et al. Decompressive surgery in cerebrovenous thrombosis: a multicenter registry and a systematic review of individual patient data. *Stroke*. 2011; 42(10):2825–2831. PMID: 21799156 https://doi.org/10.1161/STROKEAHA.111.615393
104. Raza E, Shamim MS, Wadiwala MF, Ahmed B, Kamal AK. Decompressive surgery for malignant cerebral venous sinus thrombosis: a retrospective case series from Pakistan and comparative literature review. *J Stroke Cerebrovasc Dis*. 2014;23(1):e13–e22. PMID: 24119368 https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.07.045
105. Theaudin M, Crassard I, Bresson D, Saliou G, Favrole P, Vahedi K, et al. Should decompressive surgery be performed in malignant cerebral venous thrombosis? *Stroke*. 2010;41(4):727–731. PMID: 20185780 https://doi.org/10.1161/STROKEAHA.109.572909

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