Cerebral venous thrombosis: Measuring thrombi and sinuses

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List of abbreviations

CSF  Cerebrospinal fluid
CT   Computed tomography
CTA  Computed tomography angiography
CVT  Cerebral venous thrombosis
ICP  Intracranial pressure
IIH  Isolated intracranial hypertension
LMWH Low-molecular-weight-heparin
MRI  Magnetic resonance imaging
MRA  Magnetic resonance angiography
ROI  Region of interest
SSS  Superior sagittal sinus
rST  right transverse sinus
IST  left transverse sinus
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Abstract

Background and purpose: Cerebral venous thrombosis (CVT) is a rare, but serious disease, commonly occurring in young to middle-aged women. It is not yet known whether sinus size and shape confers a risk for thrombosis and whether clot size is correlated with recanalization rates, and because there is no established method for measuring sinus or clot size, we decided to develop one.

Patients and methods: CVT patients with 3-D magnetic resonance imaging done early for diagnosis and follow-up imaging around 6 months or later were recruited. Age and sex-matched (1:2) control subjects were patients with various benign headache problems who underwent 3D MRI for excluding CVT or other acute structural disease. All major sinuses were measured in size (area and diameter). All detected clots underwent similar measurement (volume, area and length). Measurements were done with Osirix-software.

Results: 25 CVT patients (17 females and 8 males) and 50 control subjects were measured. Volume of the thrombus was either dissolved or reduced in all except one case. Sinus area in CVT patients in follow-up imaging was slightly smaller compared to healthy subjects (P=0.052-0.170). Thrombus volumes were bigger (P=0.009) but also dissolved more effectively in women, with no difference in sex-groups in follow-up imaging. Residual clot volume was bigger in older patients (P=0.007). Other factors did not strongly correlate with thrombus volume. Measurement reproducibility with two individual investigators was good, with best interrater correlation of over 95% in volume measures.

Conclusions: This is the first attempt in establishing a volumetric measurement of cerebral sinuses and clots. The methodology may help in estimating probability of recanalization and in trials with interventions such as local thrombolysis and thrombectomy.

Keywords

cerebral venous thrombosis, clot, clot size, sinus, sinus size, measurement
Review of the literature

Anatomy

Cerebral venous thrombosis (CVT) occurs when the cerebral veins or dural venous sinuses of the brain are occluded with thrombotic material. Cerebral veins emerge from the brain, run in the subarachnoid space and pierce the arachnoid membrane and meningeal layer of dura into the dural sinuses. These sinuses are located between the layers of dura mater and contain no valves or tunica muscularis. They also receive blood from diploic, meningeal, and emissary veins. Cerebrospinal fluid is absorbed from the subarachnoid space to the sinuses via arachnoid granulations. The venous drainage of the brain can be divided into superficial and deep systems. Superficial system includes the superior and inferior sagittal sinuses and cortical veins, draining mostly the superficial surfaces of cerebral hemispheres. Deep system includes the transverse sinuses, sigmoid sinuses, straight sinus, and the deeper cortical veins. It drains the deep white and gray matter surrounding the lateral and third ventricles and basal cisterns. Venous blood usually drains into the nearest sinus, or in the deeper structures, to the deep veins. Straight sinus is formed by the inferior sagittal sinus and the great vein of Galen and ends in the confluence of sinuses located at the internal occipital protuberance. Superior sagittal sinus begins just behind the frontal sinuses and courses all the way to the confluence of sinuses running in the shallow groove on the midline of the cranium. Right and left transverse sinuses leave the confluence running between the attachments of the tentorium, then drain to bilateral sigmoid sinuses which converge with the inferior petrosal sinuses and ultimately the blood leaves the brain mostly via internal jugular veins. (1,2) The anatomy of the dural sinuses is subject to great deal of variation. For example the transverse sinuses are not equal in size, the right one usually being larger and receiving majority of
the drainage from the superior sagittal sinus. The left transverse sinus Conversely receives predominantly the drainage from the straight sinus. (1,3)

Figure 1. Anatomy of the cerebral venous system (4).

Pathophysiology

Venous flow of the brain is impaired both locally and systemically when the cerebral veins or the dural sinuses are occluded with thrombotic mass leading to congestion within the venous vasculature. Localized venous infarction and edema, both cytotoxic and vasogenic, may be present. Petechial hemorrhages may develop into larger hematomas and complicate the situation. With occlusion of the major dural sinuses intracranial hypertension is explained by the impaired absorption of the cerebrospinal fluid and increased venous pressure. (5)
Epidemiology

Cerebral venous thrombosis is a rare event, the incidence being 3-4 per 1 million population annually. Young adults and children are most often affected and about 75% of the patients are women. Mean age of the patients is ~35-40 years. (5-7) SSS and the transverse sinuses are the most commonly affected sinuses. Often more than one sinus is occluded. (8)

Risk factors and etiology

The risk factors for the CVT are mostly similar to other venous thromboses and there are numerous suggested etiologies for sinus thrombosis (Table 1). The gender-specific risk factors such as use of oral contraceptives, hormone replacement therapy, pregnancy, and puerperium are markedly associated with CVT. (9) As high as 76% of women in reproductive age with sinus thrombosis may have these definable gender-specific risk factors. (10) The most common acquired risk factors are malignancies, local and systemic infections, hematologic conditions, and mechanical injury. (5,8) Several congenital risk factors, such as prothrombin G20210A mutation, activated protein C resistance, Factor V Leiden, and hyperhomocysteinemia are also associated with sinus thrombosis. (11) In 10-15% of patients no risk factor can be identified. (5,8)
Table 1. Risk factors and etiology

**Genetic thrombophilias**
- Antithrombin III deficiency
- Protein C and S deficiency
- Factor V Leiden mutation (FVR506Q)
- Prothrombin gene mutation (G20210A)
- Hereditary homocysteinemia / homocysteinuria
- Factor XII gene polymorphism

**Acquired thrombophilias**
- Antiphospholipid antibodies
- Hyperhomocysteinemia
- Nephrotic syndrome
- Pregnancy and puerperium
- Increased Factor VIII concentration

**Hematological disorders**
- Primary and secondary polycytemia
- Essential thrombocythosis
- Leukemias
- Lymphomas
- Anemias (iron deficiency, Sickle cell, thalassemia, and others)
- Paroxysmal nocturnal hemoglobinuria
- Use of erythropoietin
- High altitude

**Infections**
- Meningitis and brain abscess
- Otitis, mastoiditis, sinusitis, tonsillitis, and dental infections
- Sepsis

**Systemic inflammatory diseases**
- Systemic lupus erythematosus
- Sarcoidosis
- Wegener’s granulomatosis
- Behcet’s disease
- Inflammatory bowel disease (ulcerative colitis, Crohn’s disease)

**Drugs and natural products**
- Oral contraceptives
- Steroids
- Cytostatics
- Talidomide
- Tamoxifen
- L-Asparaginase
- Estrogen-like substance including phytogenics

**Local and mechanical causes**
- Brain tumors
- Arteriovenous malformations
- Neurosurgical operations
- Lumbar puncture
Symptoms

The most common symptom is headache, which is present in 70-90% of patients. There is no specific uniform pattern of headache for CVT but it is usually acute or subacute slowly progressing over a few days. However, an acute thunderclap-like headache is possible, too. (12) Sometimes headache can be the only sign of CVT. (13) In approximately half of the patients there are focal neurological signs. (14) Seizures are present in 40% of the patients of which 7% in acute phase. (15) In patients with isolated intracranial hypertension, the most important symptoms are headache, papilledema, nausea, and vision impairments. Isolated intracranial hypertension may be the only sign of the CVT in some cases. (16)
Diagnostics

Diagnosis of sinus thrombosis is challenging as clinical symptoms vary and neuroimaging may sometimes be difficult to interpret. Unenhanced CT-scan may show so-called cord sign (hyperdense thrombosed vein) or dense dural sinus sign (Figure 2). These are, however, relatively insensitive signs of sinus thrombosis. The empty delta sign, a more sensitive sign of CVT seen on contrast enhanced CT, may be more useful. (17) The indirect signs of CVT can also be seen on CT-scan, such as edema, decreased ventricular size or venous infarction (hemorrhagic or nonhemorrhagic). Overall, in cases of confirmed CVT, some signs of thrombus mass can be seen in unenhanced CT in 73% of the patients with no false-positive readings. (18) CT-venography is a significantly better way for CVT-diagnostics and can directly visualize sinus thrombi as filling defects. (19)

MRI and MR-venography are, however, usually the preferred initial diagnostic tests when CVT is suspected. In regular MRI, thrombus may be directly visualized and normal dural sinuses (Figure 1) are often seen as flow voids. The empty delta sign is often visible in contrast-enhanced MRI. The indirect signs are also usually better seen in MRI compared to CT. (19) In MRI thrombus, missing flow, and parenchymal changes are often easily seen. (19) MR-venography and CT-venography are probably equally sensitive in diagnosis of CVT. MRI-based techniques are often better suited for differential diagnostics and evaluating the parenchymal changes. Further, MRI is more helpful in excluding other brain pathologies. (14)

Measuring D-dimer may be useful for diagnostics. D-dimer levels have both high specificity and sensitivity in diagnosing CVT and also correlate with the extent of the disease. However, normal D-dimer cannot be used safely to rule out DST in cases of low clinical probability, as is the case in e.g. deep vein thrombosis. (20)
Figure 2. Examples of CVT-diagnostics. A. Bilateral dense dural sinus sign in transverse sinuses in unenhanced CT. B. Empty delta sign in superior sagittal sinus in contrast-enhanced CT. C. Thrombus mass seen in superior sagittal sinus in CT-venography. D. Thrombosed transverse sinus in contrast-enhanced T1 multiplanar reconstruction MRI-image. E. Cortical vein thrombus in T2*-MRI. F. MR-venography with thrombosed SSS.
Treatment

Immediate anticoagulation must be employed as the primary treatment to promote dissolving of the thrombus, to prevent rethrombosis or thrombus propagation, and to prevent pulmonary embolism even in cases with hemorrhagic changes in the brain. Anticoagulation treatment for CVT is widely considered safe and potentially effective. No new symptomatic intracerebral hemorrhages were reported in a recent Cochrane review including two studies. (21) Unfractioned intravenous dose-adjusted heparin and subcutaneous fixed dose low-molecular-weight heparin (LMWH) can both be used. LMWH should be preferred as it is more easily administered in practice and has fewer bleeding complications. Advantages of intravenous heparin include possibility of rapid discontinuation if needed. The exact duration of the anticoagulation treatment after the acute phase is also controversial. If the CVT is due to a clearly transient risk factor, such as pregnancy, oral anticoagulation may be given for 3 months. In idiopathic cases treatment of 6-12 months is recommended and continuous oral anticoagulation when a significant persistent risk factor can be identified or CVT recurs. (22)

In cases with poorer prognosis a more aggressive treatment may be beneficial. Local thrombolysis using microcatheter and recombinant tissue plasminogen activator or urokinase has shown some effect in clinical studies but also carries a higher risk of bleeding complications. It has been recommended for patients at a high risk or clinically deteriorating despite anticoagulation treatment and without intracranial hemorrhage or impending herniation. (22) Mechanical thrombectomy has also been used in selected cases. (23)

Antiepileptic treatment is used for patients with seizures. Prophylactic antiepileptic treatment may also be used in patients with certain risk factors, such as focal deficits, thrombosis of the SSS or cortical veins, and supratentorial parenchymal lesions. (15) A
prolonged treatment of 1 year can be used after the acute phase for patients with early seizures and hemorrhagic lesions. (22)

Other treatment includes sufficient fluid treatment, analgetics and treatment of elevated intracranial pressure. When anticoagulation treatment does not decrease elevated ICP, general principles of therapy should be applied (head elevation, hyperventilation, and osmotic diuretics). Acetazolamide, lumbar puncture with CSF removal, shunts, and optic nerve fenestration may be used when vision is impaired. (22) In more serious cases with threatening herniation (major cause of death in CVT), decompressive craniectomy and/or hematoma evacuation can often be lifesaving and may result in good recovery. (24)

**Prognosis**

Prognosis has improved during the last decades: total mortality rate is under 10% and below 6% during acute phase. (25) Over half of the patients have no residual symptoms at all and less than 5% are moderately impaired or severely handicapped. Most common residual symptoms are focal deficits, residual headache, and mild cognitive impairment. (8,26) Recurrence of CVT is rare, occurring in less than 3% of the cases. Incidence of other thromboembolic events (outside cerebral venous system) is under 4% among CVT-patients (25).
Aims of the study

1. To develop methodology for measuring size of cerebral veins and size of thrombus residing in cerebral veins;

2. To analyze whether size of thrombus predicts recanalization and severity of symptoms; and

3. To analyze whether size of cerebral veins in patients with CVT differ from those in healthy subjects.

Patients and methods

This study was approved by the relevant authorities and carried out at the Department of Neurology, Helsinki University Central Hospital. We searched all patients with angiographically verified diagnosis of CVT between 1990-2010. Only patients with high quality MRI-images in both acute and follow-up phase (usually 6 months) were included to ensure precise measurements. Control population consists of age- and sex-matched patients imaged for headache or other neurological symptoms for excluding CVT but with no findings related to CVT. The MRI-images of the patients and control subjects were transferred to DVDs in DICOM-format from the hospital's electronic image archives. All the measurements were made with Osirix program (version 3.8.1) in Mac Os X-environment (http://www.osirix-viewer.com/) and usually from multi planar reconstruction (MPR) images. Measuring the cortical thrombus was especially challenging and they were sometimes better visualized in T2*-images. MR-images of the acute phase and the follow-up images (usually collected six months after the acute phase) were both measured for all patients. All the measurements were made by the same researcher. To
assess interrater reproducibility, blinded measurements using the same method were performed by a second investigator for a random set of 10 patients.

Volumes of the thrombi were measured in CVT-patients in SSS, sinus transversus, straight sinus, and cortical veins. Area and length of the thrombi were measured in SSS, sinus transversus and straight sinus. In CVT-patients and in control subjects area of the actual sinus was measured in SSS, sinus transversus, and straight sinus. The diameter of the SSS was measured in control subjects and in the follow-up images of the CVT-patients.

All the measurements regarding SSS and straight sinus were made from sagittal slices. Transverse sinuses, sigmoid sinuses and internal jugular veins were measured from transverse slices. When cortical thrombi were present, they were usually measured from transverse slices. Confluence of the sinuses was in these measurements considered as part of the SSS. Volume of the thrombus in transverse sinuses also includes thrombus mass in the sinus sigmoideus and internal jugular vein. Area and length of the thrombus in sinus transversus, however, only includes the part of the thrombus in the actual sinus transversus.
Figure 3. Thrombus mass in right transverse sinus outlined in one slice.

Volumes of the thrombi were measured by manually outlining the area of the actual thrombus mass in each individual slice using the “Closed polygon” tool (Figure 3). Subsequently, volume of the thrombus was computed with “ROI Volume” tool by the program. Area of the thrombus and the area of the actual sinus were measured using also the “Closed polygon” tool by manually outlining the desired area (Figure 5), and when needed, constructed from several slices (for example in the case of SSS usually from 1-3 adjacent sagittal slices). Length of the thrombi were measured using the “Length” tool by drawing several straight lines running approximately in the middle of the thrombus mass and when needed measured from adjacent slices as when measuring the area. The diameter of the actual SSS was measured with “Length” tool at the highest point of the SSS, in the middle between the highest point and the starting point of the SSS and in the middle between the highest point and the confluence of sinuses (Figure 4).
Figure 4. Diameters of the SSS in three established measurement points

Figure 5. Area of the superior sagittal sinus outlined in a healthy control subject.
SPSS statistics 20 was used for statistical analyses (IBM Corporation, 2011). Mann-Whitney-U and Kruskal-Wallis tests were used to analyze differences of sinus measurements between patients and controls, and differences of thrombus volume in patient subgroups. Wilcoxon signed rank test was used for related samples. Measurement reproducibility was assessed by comparing means of the two individual investigators, correlation over 95% was desired. Two-sided values of $P<0.05$ were considered statistically significant.

The role of the researcher (H.H) in this study was to develop methodology to measure dural sinuses and the thrombi residing in them as there was no existing methodology to do this. MRI-images were transferred and evaluated by the researcher to determine whether they were of good enough quality to make accurate measurements. Radiologist's MRI-reports of the images and consultations from a neuroradiologist were used as an aid when needed. All the measurements were made by the same researcher with same equipment and applying same methods.
Results

Measurements were done for a total of 25 CVT-patients in both acute and late phase. Mean age of the patients was 43.6, and mean age for women (17 in total) was 40.6 and for men (8 in total) 50.0. We have 50 control patients with the mean age of 44.1. Mean age for women (34 in total) was 41.7 and for men (16 in total) 49.2, e.g. 2 age- and sex-matched control subjects for every CVT patient.

Measured sinus areas in patients (follow-up images) and control subjects are compared in table 2. The control patients had a slightly larger sinus size, however, the difference was not statistically significant. Area of the sinuses in CVT patients was significantly bigger in acute phase than in the follow-up imaging (Table 3).

Table 4 represents the thrombus volumes in different patient groups in both the acute and follow-up phase. Thrombus volumes were either reduced or totally dissolved in all patients with one exception where the thrombus volume was bigger in follow-up phase. Women had significantly larger thrombus volumes in the acute phase. However, in the follow-up images there was no difference in the thrombus volume. In the older age group (cut-point 44 years) the residual thrombus volume in follow-up phase was significantly bigger with no difference in the acute phase compared to younger age group. Otherwise the risk factors, clinical presentation, the parenchymal lesions in MRI imaging or the outcome did not correlate with thrombus volume.

Measurement reproducibility was investigated with two individual investigators, interrater correlation of thrombus volume and sinus volume measures was over 95% in all measurement points. In thrombus length and thrombus area measurements interrater correlation was over 95%. Sinus area measurement correlation was 87% in right transverse sinus, 88% in straight sinus and 95% in left transverse sinus. Lower correlation was achieved in SSS diameter measurements; anterior 54%, superior 87% and posterior 77%.
Table 2 Sinus size in cerebral venous thrombosis patients and in control subjects

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<tr>
<td></td>
<td>mean</td>
<td>range</td>
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<td>Area (cm²)</td>
<td></td>
<td></td>
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<td>17.16</td>
<td>12.39-22.82</td>
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<td>Right sinus transversus</td>
<td>5.39</td>
<td>3.72-8.55</td>
<td>5.74</td>
<td>2.17-8.47</td>
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<td>Left sinus transversus</td>
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<td>1.76-6.39</td>
<td>4.73</td>
<td>2.63-7.95</td>
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<td>Rectus</td>
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<td>1.44-3.86</td>
<td>2.75</td>
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<td>Superior sagittal sinus diameter (cm)</td>
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<tr>
<td>Anterior</td>
<td>0.42</td>
<td>0.30-0.57</td>
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<td>Middle</td>
<td>0.90</td>
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<td>0.97</td>
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<td>Posterior</td>
<td>0.69</td>
<td>0.52-0.96</td>
<td>0.70</td>
<td>0.49-1.01</td>
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Table 3 Sinus and thrombus area and thrombus volume changes in the acute and follow-up imaging

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<th>Follow-up</th>
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<td><strong>Sinus Area (Cm²)</strong></td>
<td>mean</td>
<td>range</td>
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<tr>
<td>Superior sagittal sinus</td>
<td>19.67</td>
<td>14.2-2.1</td>
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<td>Transverse sinus, right</td>
<td>6.07</td>
<td>3.4-9.4</td>
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<tr>
<td>Transverse sinus, left</td>
<td>4.84</td>
<td>2.2-8.0</td>
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<tr>
<td>Straight sinus</td>
<td>3.21</td>
<td>2.0-5.9</td>
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<td><strong>Thrombus Area (Cm²)</strong></td>
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<tr>
<td>Superior sagittal sinus, n=15</td>
<td>4.12</td>
<td>0.3-11.1</td>
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<tr>
<td>Transverse sinus, right, n=17</td>
<td>2.43</td>
<td>0.0-6.1</td>
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<tr>
<td>Transverse sinus, left, n=10</td>
<td>2.49</td>
<td>0.6-4.3</td>
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<td>Straight sinus, n=5</td>
<td>1.64</td>
<td>0.5-3.1</td>
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<td><strong>Thrombus volume (Cm³)</strong></td>
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<td>Total, n=25</td>
<td>4.59</td>
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<tr>
<td>Superior sagittal sinus, n=15</td>
<td>2.23</td>
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<td>Transverse sinus, right, n=17</td>
<td>3.32</td>
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<td>1.81</td>
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<td>Cortical veins, n=6</td>
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<td>0.3-1.2</td>
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**Table 4.** Thrombus volume measurements in different patient groups in the acute and follow-up imaging

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<th>Thrombus volume at follow up (cm³)</th>
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<td>Female</td>
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<tr>
<td>Age</td>
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<tr>
<td>&lt;44 years</td>
<td>4.77</td>
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<tr>
<td>≥44 years</td>
<td>4.31</td>
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<td>Acute</td>
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<td>Subacute</td>
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<td>Chronic</td>
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<td>MRI Imaging</td>
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<td>No parenchymal lesions</td>
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<td>Parenchymal lesion(s)</td>
<td>2.43</td>
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<td>Clinical presentation</td>
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<td>Isolated headache</td>
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<td>Focal symptoms</td>
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<td>Impaired consciousness</td>
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<td>Risk Factors</td>
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<td>≥1 identified risk factor(s) (n=14)</td>
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</tr>
<tr>
<td>Good recovery (mRS 0-1) (n=16)</td>
<td>4.69</td>
<td>0.62</td>
</tr>
<tr>
<td>Incomplete recovery (mRS&lt;2) (n=3)</td>
<td>1.84</td>
<td>0.12</td>
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</table>
Discussion

Cerebral venous thrombosis is a rare disease with various manifestations and is usually difficult to diagnose. With improved early diagnosis and quickly started treatments, the prognosis of the disease has clearly improved and mortality rates are already below 10%. However, considering that most patients are rather young and many survive with significant morbidities, there is still room for enhancing both diagnostics and treatment modalities.

There exists no previous work attempting at measuring clot size in CVT patients. Therefore, there are no data describing whether large thrombi remain without recanalization, lead to more severe consequences, and long-term disabilities. If large thrombi are associated with dismal outcomes, then, novel approaches e.g. local thrombolysis or surgical removal of thrombus from superficial sinuses may be warranted. These high-risk interventions often require an early estimate of likelihood of spontaneous recanalization and measurement of clot size.

One previous study investigated the cerebral venous volume in patients with idiopathic intracranial hypertension (27). In that study volume measurements were taken from reconstructed 3D images from MRV images without contrast. Therefore the methodology differed from ours. In our method manually approximating the thrombus matter in sinuses does not suffer from bias caused by slow blood flow and noncontinuous thrombus matter.

Another unexplored issue is whether the size of the cerebral sinuses differs significantly among adult individuals and whether size of the sinuses might be a factor predisposing to thrombosis. Because the sinus size cannot be measured reliably upon presence of thrombus in it, we considered only patients with recanalization at 6 or 12 months post-thrombosis presuming that sinus size returned to its original size at this point of time. For this part of the study, we recruited age- and sex-matched patients who underwent brain
MRI for various headaches and imaging excluded CVT as well as other serious brain pathology.

The trend of CVT patients having smaller sinus size in control imaging compared to healthy control subjects could be an undiscovered risk factor for CVT combined with other prothrombotic factors. However, it did not reach a statistical significance and could reflect reactive shrinkage in exposing these individuals to different venous blood flow conditions, or merely a chance finding. Significance of this is finding should be studied more extensively.

Thrombosed sinuses were clearly engorged in the acute phase followed by significant reduction in sinus size after total or partial recanalization. Theoretically this could be explained by recanalization of the occluded sinus resulting in lessening the flow obstruction and venous congestion.

The more effective dissolving of the thrombus in women may be related to the fact that gender-specific risk factors play a bigger role in women with CVT, namely contraceptive pill, HRT, pregnancy, and puerperium. These are often transient and easily treated compared to other risk factors. Similarly the finding of greater residual volume of the thrombus in older age group may reflect the smaller role of these transient risk factors in these patients.

In previous studies the correlation between outcome and recanalization has been unclear. Some studies have found no correlation (28) and some have reported higher frequency of residual symptoms or worse outcome with no recanalization (29,30). In this study there was no correlation between outcome and residual thrombus volume or volume change. The lack of correlation between thrombus size and risk factors or clinical factors in this study may be due to a small sample size and should be investigated in a larger population.

Our work has certain limitations. Firstly, the number of patients is rather small. Secondly, sinus size at 6 or 12 months post-CVT may still be different from its original size. Thirdly,
there is no well-established gold standard methodology for measuring thrombus or sinus size. These results should therefore be considered as hypothesis-generating. Volumetric studies done manually are naturally also prone to errors, but in this study the correlation between individual measurers using the same methodology was good, the highest reproducibility found in volume measurements. These volume measurements have more dimensions and attempt to measure the actual real-life clot size compared to more rater-dependent and less objective area and length measurements. However, this study also has certain strengths. Firstly, it brings a novel approach in evaluating CVT patients. Secondly, all calculations were done on state-of-the-art MR images.

Larger studies investigating the sinus and thrombus volumes and the possible implementation to clinical practice are warranted to reveal significance of our method and findings. Manual measurements used in this study are time-consuming but also likely more reliable compared to automated calculations, especially when implementing a novel method. One possibility could be a user-supervised reliable automated software developed for measuring the sinuses and the clots.
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