Isolated Cortical Vein Thrombosis
Systematic Review of Case Reports and Case Series

Jonathan M. Coutinho, MD, PhD; Jorn J. Gerritsma, MSc; Susanna M. Zuurbier, MD; Jan Stam, MD, PhD

Background and Purpose—Isolated cortical vein thrombosis is a distinct subtype of cerebral venous and sinus thrombosis. Because of the rarity of isolated cortical vein thrombosis, limited knowledge on its clinical and radiological manifestations is available.

Methods—We performed a systematic review of published data. Isolated cortical vein thrombosis had to have been diagnosed by MRI, conventional angiography, computed tomography venography, autopsy, or surgery. Cases with concurrent thrombosis of a cerebral sinus were excluded.

Results—Of 175 potentially relevant studies, 47 were included in the analysis, with a total of 116 patients. All studies were case reports and case series. Mean age was 41 years and 68% were women. The most common symptoms were headache (71%), seizures (58%), and focal neurological deficits (62%). Papilledema was not reported in any patient, and increased cerebrospinal fluid pressure was reported only in 2. Infection (19%), pregnancy or puerperium (35% of women), and oral contraceptive use (21% of women) were the most common risk factors. Most cases (73%) were diagnosed with MRI, but conventional angiography was also performed in 47%. A total of 81% had a parenchymal brain lesion and 80% were treated with anticoagulation. In-hospital mortality was 6%.

Conclusions—Signs of increased intracranial pressure seem to be less common in isolated cortical vein thrombosis compared with cerebral venous and sinus thrombosis. MRI and in some cases conventional angiography are the most frequently used diagnostic modalities and anticoagulation is the most widely used therapy. (Stroke. 2014;45:1836-1838.)

Key Words: review, systematic ■ sinus thrombosis, intracranial ■ stroke

Thrombosis of the cerebral cortical veins is mostly seen in conjunction with thrombosis of a major cerebral sinus (cerebral venous and sinus thrombosis [CVST]). Isolated cortical vein thrombosis (ICVT) is rare and has been reported only in case reports.1 Because of the paucity of data, little is known about its clinical manifestations, treatment, and outcome. The aim of the current study was to perform a systematic review of published cases on ICVT.

Methods
We searched Medline, Excerpta Medica Database (EMBASE), and Current Index to Nursing and Allied Health Literature (CINAHL) (until July 1, 2013) for publications on ICVT (adult and pediatric cases), using the terms cortical vein thrombosis and cortical venous thrombosis. In addition, we searched EMBASE and Web of Science for relevant conference abstracts and the grey literature (www.opengrey.eu). The primary search was performed by 1 author (J.J.G.). Full-length articles of potentially relevant publications were reviewed independently by 2 of the authors (J.M.C. and J.J.G.). In situations of disagreement, a third author (J.S.) made the final decision. We also screened reference lists of included articles for additional relevant studies. ICVT had to have been diagnosed by MRI, conventional angiography, computed tomography venography, or at surgery or autopsy. Cases with concurrent thrombosis of a cerebral sinus or with isolated thrombosis of the deep venous system were excluded. Studies describing both CVST and ICVT cases were included if the required data from the patients with ICVT could be extracted. Articles written in languages other than English, French, German, Spanish, Portuguese, or Dutch were only selected if they had an English abstract with sufficient data.

Results
We identified 1092 publications, of which 175 were selected for full-length review. Of these, 47 articles fulfilled the inclusion criteria. All studies were case reports or case series, describing 1 to 32 cases per publication (Table I in the online-only Data Supplement). In total, we found 116 patients with ICVT. The mean age of patients was 41 years and 68% of patients were women (Table 1). There were 3 pediatric cases (1 neonatal). The median interval from symptom onset to diagnosis was 7 days (mean, 23 days). Seventy-one percent of patients reported headache, 58% had seizures, and focal neurological deficits were present in 62%. Fundoscopy was performed in 48 patients; none of these patients had papilledema.
Table 1. Clinical Characteristics and Risk Factors

| Demographics          | n/N (%)*
|-----------------------|--------
| Mean age, y (SD)†     | 41 (17)
| Sex (% of women)      | 55/81 (68%)

| Clinical characteristics | n/N (%)*
|--------------------------|--------
| Median duration symptom onset, diagnosis (IQR)‡ | 7 days (3–16)
| Median duration admission, diagnosis (IQR)§ | 3 days (0–10)
| Headache                   | 76/107 (71%)
| Papilledema               | 0/48 (0%)
| Seizures                  | 67/116 (58%)
| Focal neurological deficit | 71/115 (62%)
| Comatose                  | 2/97 (2%)

| Risk factors                           | n/N (%)*
|----------------------------------------|--------
| Oral contraceptive use (% of women)    | 8/39 (21%)
| Pregnancy or puerperium (% of women)   | 15/43 (35%)
| Infection                              | 18/95 (19%)
| Genetic thrombophilia                  | 10/107 (9%)
| Lumbar puncture                        | 14/86 (16%)
| Malignancy                             | 5/109 (5%)

IQR indicates interquartile range.

*Categorical variables are given as n/N, where n is the number of patients in which the variable was present and N the total number of patients for which that particular variable was reported.
†Calculated from data of 81 patients.
‡Calculated from data of 41 patients.
§Calculated from data of 42 patients.

Oral contraceptive use (21% of women), pregnancy or puerperium (35% of women), infection (19%), and lumbar puncture (16%) were the most common risk factors.

Almost all patients underwent MRI of the brain (Table 2). In 73% of patients, MRI established the diagnosis of ICVT. Conventional angiography was performed in 47%. Thirteen patients (21%) underwent lumbar puncture as part of the diagnostic work-up and only 2 had an increased cerebrospinal fluid (CSF) pressure. Both these patients also had large cerebral lesions with mass effect. Eighty-one percent of patients had increased CSF pressure. Both these patients had a large sinuses is not affected, intracranial hypertension is less likely to occur. The absence of papilledema in these cases and the lower frequency of headache would support this hypothesis. Furthermore, although increased CSF pressure is a common finding in patients with CVST,3 only 2 of 11 patients with ICVT had increased CSF pressure. Both these patients had a large venous infarct, which might explain the increased CSF pressure. Unfortunately, the large amount of missing data on papilledema and CSF pressure makes it difficult to draw definitive conclusions on the frequency of intracranial hypertension in ICVT.

A parenchymal brain lesion (localized edema, hemorrhagic infarct, or intracerebral hemorrhage) was present in almost all patients with ICVT, compared with 28% of patients with CVST.

Headache was also less common in ICVT (71% versus 89%), although still present in most cases. The almost invariable presence of headache in CVST is partly explained by intracranial hypertension. Because in ICVT the venous outflow through the large sinuses is not affected, intracranial hypertension is less likely to occur. The absence of papilledema in these cases and the lower frequency of headache would support this hypothesis.

Discussion

This is the first systematic review of the literature on ICVT. Comparison of our data with the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) shows that the clinical manifestations of ICVT largely coincide with those of CVST.2 However, papilledema was not reported in any
MRI was the most frequently used imaging method, especially in contemporary studies. Although we lacked data to determine whether computed tomography venography is insufficient to diagnose ICVT, this imaging technique was used rarely. When MRI is performed, a T2*-gradient echo sequence should be included because this is the most sensitive technique to demonstrate the presence of a thrombus in a cortical vein. In difficult cases, however, even MRI can be nondiagnostic, and conventional angiography may still be required.

It seems prudent to extrapolate the guidelines on the treatment of CVST to patients with ICVT. Anticoagulation with therapeutic doses of heparin therefore seems to be the standard of care, as was used in most patients. In rare cases where impending herniation occurs, decompressive craniectomy should be performed, similar to CVST. Endovascular thrombolysis does not seem to be an option because the cortical veins cannot be reached with a microcatheter without a high-risk perforation. The in-hospital mortality of 6% in the published cases is similar to the mortality in CVST (4.3% in the ISCVT study). Death most often occurred in patients with an infection of the central nervous system, which is also an established risk factor for poor outcome in CVST.

An important limitation of our study is that we only identified case reports and case series. As a result, publication bias is a probable confounder and the data must be interpreted with caution. For instance, 16% of the patients developed ICVT after lumbar puncture, mostly after epidural anesthesia. Although lumbar puncture is a known risk factor for CVST or ICVT, it is improbable that this percentage is an accurate estimate. Instead, it is much more likely that these patients are over-represented in the literature because neurological complications are among the most-feared complication of epidural anesthesia.

In conclusion, our systematic review suggests that signs of increased intracranial pressure are less common in ICVT compared with CVST, whereas localized cerebral edema or hemorrhagic lesions are more frequent in ICVT. MRI and conventional angiography are the most frequently used diagnostic modalities, and anticoagulation is the most widely used therapy.

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Disclosures
None.

References
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## Supplemental material

### Table I: study characteristics

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*Only the number of patients with ICVT is provided. The original publication may describe additional patients. DSA = digital substraction angiography
References of included studies


