Journal of Clinical Neuroscience xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Review article

Outcomes in adults with cerebral venous sinus thrombosis: A retrospective cohort study

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ARTICLE INFO

Article history:
Received 24 January 2018
Accepted 11 March 2018
Available online xxxx

Keywords:
Cerebral sinus thrombosis
Cerebral venous sinus thrombosis
Complications
CVST
Dural venous sinus thrombosis

ABSTRACT

Most patients with cerebral venous sinus thrombosis (CVST) treated with anticoagulation have good outcomes. We examined which factors were associated with poor outcomes after treatment. We retrospectively reviewed patients ≥18 years old who were diagnosed with CVST between 1997 and 2015. Good (modified Rankin score [mRS] ≤2) and poor outcomes were dichotomized. Demographic, historical, clinical, imaging, and treatment characteristics were compared. Eighty-nine patients received treatment for CVST (52.8% males, 74.2% Caucasian). Sixty-eight (76.4%) had good outcomes and 21 (23.6%) had poor outcomes. Poor outcome was associated with systemic or central nervous system (CNS) infection (p = 0.002), lower use of heparin-only therapy than interventional-only treatments (p = 0.003), and increased use of craniectomy (p = 0.002). Good outcomes were associated with migrainous headache on presentation (p = 0.01) and involvement of superficial cortical vessels only (p = 0.02). No prothrombotic or imaging findings correlated with poor outcome. Multivariable analysis showed that any clinical risk factor (p = 0.02) and headache (p = 0.02) predicted improved outcome whereas systemic or CNS infection (p = 0.02) and craniectomy (p = 0.02) predicted poor outcome. A published risk score showed a moderate ability to predict good outcome but not poor outcome. Overall sensitivity (23.8%), specificity (75.0%), and positive (24.0%) and negative (77.0%) predictive value suggested moderate prediction of good outcome and limited prediction of poor outcome. Rates of poor outcomes in CVST were comparable with previous investigations (23.6%), but prediction of poor outcome remains challenging in patients with CVST. Our results suggested that systemic infection and craniectomy were the most robust predictors of poor outcome.

1. Introduction

The incidence of cerebral vein and dural sinus thrombosis (CVST) is estimated to be between 0.2 and 1.57 per 100,000 per year; CVST represents between 1 and 5% of all strokes [1–3]. Patients can present with headache, focal neurological deficit, or seizure. Predisposing factors include hypercoagulability, cancer, medications, and infection. CVST is typically treated with anticoagulation. Prognosis is favorable in about 75% of patients [3,4]; however, with clinical decline and poor prognosis in about 25% of patients, earlier prediction of patient prognosis would be helpful in closer management and more aggressive treatment. In addition to the predisposing factors described above, a number of risk factors for poor outcomes in CVST have been proposed [5–14], and various prediction tools have been suggested with one formalized as a risk score [2]. Because clinical prediction of prognosis after CVST diagnosis remains challenging, we hypothesized that specific risk factors could be identified in our patients that would accurately predict prognosis. We sought to identify these factors and assess the predictability of an available risk model.

2. Materials and methods

2.1. Patient selection

After obtaining institutional review board approval, we retrospectively reviewed the medical records of inpatients enrolled from January 1997 to December 2015 in the University of Utah Stroke Center Database and a separate neurosurgery departmental

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https://doi.org/10.1016/j.jocn.2018.03.004
0967-5868/

database. Patients with the diagnosis of spontaneous CVST were identified by a manual review of the patients' electronic medical records. Patients were included if they were over 18 years old and had complete demographic, clinical, imaging, hypercoagulability workup, treatment, and outcome data. Patient outcome was retrospectively assessed at last known clinical follow-up or a total of 1 year, whichever was longer. The primary outcome was modified Rankin scale (mRS); good and poor clinical outcomes were defined as a score of 0–2 or 3–6, respectively.

2.2. Analysis

Demographic data collected was age at time of CVST, sex, and race. We searched available electronic clinical records made at the time of hospitalization and during clinical follow-ups. Evaluated pre-CVST history included travel history; history of thrombosis, ischemic stroke, myocardial infarction, intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), miscarriage, pregnancy, obesity, systemic or central nervous system (CNS) infection, cancer, or trauma; recent surgery; estrogen exposure; and smoking. Clinical factors at time of presentation that were examined included the presence of headache (migraine or non-migraine type headaches as per the International Classification of Headache Disorders), clinical signs of dehydration (e.g., hypotension, tachycardia), altered mental status, coma, aphasia, mono-/hemiparesis, seizure, nausea/emesis, blurred vision, diplopia, papilledema, and ataxia. The severity of symptoms was not assessed for this study. If a history of a clinical factor was not mentioned in the clinical records, it was presumed to not be present. Imaging data collected included treatment modalities used (computerized tomography [CT] and CT angiography [CTA]; magnetic resonance imaging [MRI] and MR angiography [MRA]; catheter-based angiography), presence of parenchymal edema, infarction, ICH, and the specific venous sinuses involved. Venous occlusion was noted if 100% occlusion was found; partial, nonocclusive thrombus was not counted. The locations of all venous thrombi were catalogued, including deep vessels (e.g., internal cerebral veins, cavernous sinus), superficial vessels (e.g., veins of Trolard and Labbé), and cerebral sinuses (e.g., superior sagittal, transverse/sigmoid, straight, torcula, jugular vein). All images were reviewed by a board-certified neuroradiologist. The severity of imaging findings (i.e., degree of cerebral edema) was not cataloged. Results of hypercoagulability laboratory results that were obtained routinely as part of a prothrombotic workup were recorded. Hypercoagulability laboratory studies were not performed in every patient and are reported as a fraction of total analyzed patients. Specific treatment modalities, including systemic anticoagulation with unfractionated or fractionated heparin, hemicraniectomy, and endovascular treatments, were collected. Endovascular treatments were broken down into those using intravenous or intrasinus heparin (IV-heparin), tissue plasminogen activator (IV-TPA), mechanical thrombolysis, or a mix.

2.3. Risk score evaluation

Patient outcomes were compared with a previously published risk scoring system [2]. The scoring system was developed from data from the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) (n = 624) to generate a risk score that was validated on the Cerebral Venous Thrombosis Portuguese Collaborative Study Group (VENOPORT) sample set (n = 91) and a second data set (n = 169). A sensitivity of 96.1% and specificity of 13.6% were reported for identifying poor outcome, defined as a mRS >2 at 6 months. The score assigned cumulative points based on hazard ratios in the model for malignancy (hazard ratio [HR] = 4.53, 2 points), coma (HR = 4.19, 2 points), thrombosis of the deep venous system (HR = 3.03, 2 points), male sex (HR = 1.6, 1 point), and intracranial hemorrhage (HR = 1.42, 1 point). Factors with the highest HRs were assigned higher weights in the scoring system based on analyzed HR. The summed points predicted outcome (% risk of poor outcome at 6 months) as follows: 0 (<5% risk), 1 (10% risk), 2 (20% risk), 3 (25% risk), and >4 (40% risk).

2.4. Statistical analysis

Distributions of continuous variables are reported as means and standard deviations and were evaluated by *T*-test. Discrete variables are reported as a percentage of the total and were evaluated by Chi-squared test. Univariable analyses were used to predict a good outcome (mRS $\leq$2), and significant variables were entered into a multivariable analysis. Sensitivity and specificity were used to analyze the risk score a cutoff value of $\geq$3 as used by Ferro et al. [2]. A p-value <0.05 was considered statistically significant. Analysis was performed with SPSS V22.0 (IBM, Armonk, NY).

3. Results

3.1. Patient characteristics

A total of 396 patients were identified in the Stroke Center Database and an internal neurosurgery database. We analyzed 89 patients in the present study who had complete data recorded, with an average group age of 46.0 ± 19.8 years (range 15–87) (Table 1). There were 47 men (52.8%). Outcomes were measured at last known follow-up post-CVST hospitalization. The average length of follow-up did not differ between good and poor outcome groups (16.0 ± 24.0 vs. 2.0 ± 3.5 months, p = 0.07).

A total of 68 patients (76.4%) had a good outcome (mRS $\leq$2) and 21 (23.6%) had a poor outcome (mRS >2). At most recent follow-up, among the patients with good outcomes, 33 patients had an mRS of 0 (48.5%), 24 patients had an mRS of 1 (35.2%), and 11 patients had an mRS of 2 (16.2%). Among patients with poor outcome, 6 patients had an mRS of 3 (28.6%), 2 patients had an mRS of 5 (9.5%), or 13 patients had an mRS of 6 (61.9%). There was no distribution difference among races (p = 0.30). More patients with good outcomes had an identifiable prothrombotic risk factor (95.6% vs. 81.0%, p = 0.03); however, of all the risk factors recorded, only infection was found at a significantly higher rate in those with poor outcomes (13.2% vs. 38.1%, p = 0.002). No significant difference in the presence of clinical symptoms at the time of diagnosis was seen between good and poor outcome groups (97.1% vs. 95.2%, p = 0.68). A higher number of patients with good outcome presented with migraine headache (25.0% vs. 14.3%, p = 0.01).

3.2. Imaging and thrombosis workup

Imaging and prothrombotic laboratory test results were compared between the two groups (Table 2). A higher number of patients in the good outcome group underwent MRI/MRA for CVST diagnosis compared with the poor outcome group (73.5% vs. 42.9%, p = 0.009); there was no difference between good and poor outcome groups in the use of CT/CTA imaging or catheter-based angiography.

No differences in the presence of cerebral edema, infarction, or ICH were seen between outcome groups. A higher rate of involvement of superficial cortical vessels (66.2% vs. 38.1%, p = 0.02) in patients with good outcomes, but otherwise there was no difference in the location of CVST between groups. The number of overall involved vessels did not differ between good and poor outcome groups (2.0 ± 2.3 vs. 2.8 ± 1.8, p = 0.1); however, the degree of partial, unobstructed vein occlusion was not measured.

Please cite this article in press as: Karsy M et al. Outcomes in adults with cerebral venous sinus thrombosis: A retrospective cohort study. J Clin Neurosci (2018), https://doi.org/10.1016/j.jocn.2018.03.004