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Letter to the Editor

Pediatric cerebral sinovenous thrombosis: Optimal treatment may differ by etiology

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To the Editor:

Cerebral sinovenous thrombosis (CSVT) can lead to long-term neurologic disability if impaired venous outflow results in cerebral ischemia or hemorrhage. Anticoagulation is the standard treatment for adults with CSVT [1,2], but the optimal treatment of children may differ due to developmental hemostasis. Consensus guidelines, which are largely extrapolated from adult data with support from case series and observational studies of children, suggest that anticoagulation should be instituted for treatment of childhood CSVT and continued for 3–6 months [3,4]. Despite mounting evidence supporting the use of anticoagulation in the treatment of childhood CSVT [4,5], studies evaluating the influence of CSVT etiology on the optimal management strategy are limited. One multicenter registry study of 396 pediatric patients with CSVT found that the risk of recurrence was dependent upon the etiology of the thrombus, and therefore, the authors suggested that prolonged anticoagulation might only be justified in certain subgroups of children [6]. Studies addressing how CSVT etiology should impact initial anticoagulation treatment strategy are even more limited.

We hypothesized that when the cause of CSVT is transient or treatable, such as in trauma or infection, anticoagulation may not be necessary, as intrinsic thrombolytic mechanisms may result in vessel recanalization in the absence of ongoing risk for clot formation and propagation. Furthermore, anticoagulation may pose higher risk after trauma or if surgery is needed, a common occurrence with both trauma- and infection-associated CSVT, when procedures such as mastoidectomy, myringotomy, and abscess drainage are commonly needed. Good neurologic outcomes have been demonstrated in children with trauma- or surgery-related CSVT who did not receive anticoagulation [7,8]. A better understanding of which children may benefit from anticoagulation and which children may be at increased risk would allow for individualized therapeutic strategies based on CSVT etiology and could improve outcomes. Therefore, in this retrospective study, we aimed to evaluate differences in treatments and clinical and radiographic outcomes based on CSVT etiology.

We used ICD-10 codes to identify pediatric patients, including neonates, with a diagnosis of CSVT at our tertiary care children's center over a 10-year period (5/2008–5/2018). Information including demographics, risk factors, presenting symptoms, treatment, and outcome was collected. In children who did not receive anticoagulation, we explored the reasons anticoagulation was deferred and compared the outcomes of children who received anticoagulation with those who did not.

Thirty patients met inclusion criteria, with mean age 7.4 years (8 days–17.6 years). Three neonates (< 28 days of life) were included in the analysis. Seventeen (57%) of our cohort were male. Common risk factors included trauma (n = 10, 33%), infection (n = 9, 30%), and hypercoagulable state (n = 7, 23%) (Table 1). Infections included mastoiditis, periauricular abscess, orbital cellulitis, sinusitis, acute otitis media, meningitis, subdural empyema, and viral upper respiratory infection.

Twenty-four children (80%) received therapeutic anticoagulation, including 5 patients who had intracranial hemorrhage (ICH) on presentation and all 3 neonates. In the 5 patients with ICH, anticoagulation initiation was delayed an average of 4.3 days (range 1–20 days) due to either surgery or decision of the treating team. In two cases, anticoagulation was initially withheld but was subsequently initiated due to clot propagation on surveillance neuroimaging. Neither child suffered a venous infarction or hemorrhage as a result of the CSVT. Anticoagulation was continued for a mean of 5.5 months (range 1.5–12 months) in children with transient or no identified risk factors. In children with life-long hypercoagulable disorders, anticoagulation was continued indefinitely. No patient developed symptomatic ICH or expansion of pre-existing hemorrhage after anticoagulation initiation. At most recent clinical follow up time of 18.5 months (range 2.6 months to 8.4 years), neurologic sequelae were present in 33%, most commonly headaches and seizures.

Six children did not receive therapeutic anticoagulation. Children who did not receive anticoagulation in our cohort were on average younger than children who did not (Table 2). Five of the six children who did not receive therapeutic anticoagulation had traumatic injuries as the cause of the CSVT, and the risk of anticoagulation was felt to outweigh potential benefits. The sixth child was started on anticoagulation but it was discontinued before reaching therapeutic levels because the child required surgical drainage of an abscess. Of these 6 children, 2 (33%) had full venous recanalization and one additional child had partial recanalization demonstrated on most recent imaging, possibly due to short interval of follow up imaging (mean 69 days, range 3–220 days from the time of diagnosis). Despite that, at mean clinical follow up time of 10 months (range 1 to 33 months), no child had suffered a venous infarction and only one child who did not receive anticoagulation had any neurologic deficit.

In this small cohort examined retrospectively, children with transient or treatable causes of CSVT, such as trauma and infection, who did not receive anticoagulation did not suffer venous infarction or hemorrhage, nor did they have worse clinical outcomes in comparison to

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Table 1
Clinical and treatment characteristics by CSVT etiology.

	Total	Traumatic	Infection	Other causes/cryptogenic
Number	30	10	9	11
Anticoagulated (%)	24 (80)	5 (50)	8 (89)	11 (100)
Mean furthest follow up time in days (range)	504 (38–365)	262 (38–994)	283 (78–882)	904 (166–3068)
Deficits at furthest follow up (%)	10 (33)	2 (20)	4 (44)	4 (36)
Full recanalization at furthest follow up	13 (43)	4 (40)	3 (33)	6 (55)
Number that propagated before anticoagulation	2	1	0	1
Venous infarctions before diagnosis, n	6	2	1	3
Venous infarctions after diagnosis, n	0	0	0	0

Table 2
Characteristics and imaging/clinical follow-up in children that received and did not receive therapeutic anticoagulation for CSVT.

	Anticoagulation	No anticoagulation
Number	24	6
Age, years (range)	7.8 (0.01–17.6)	5.5 (0.9–13.5)
Male, n (%)	14 (58)	3 (50)
Time to most recent clinical follow-up, months (range)	18.5 (2.6–102.3)	10 (1 − 33)
Neurologic sequelae at follow-up, n (%)	8 (33)	1 (17)
Full recanalization demonstrated on most recent imaging, n (%)	11 (46)	2 (33)

children treated with anticoagulation. However, concordant with prior studies, anticoagulation did not result in neurologic complications even in children with traumatic head injuries and concurrent ICH.

Though our sample size is too small to make any definitive conclusions, we believe these data suggest that further exploration of optimal treatment strategy stratified by CSVT etiology is needed. In particular, studies aimed at defining a subpopulation of children with CSVT in whom withholding anticoagulation is the safest option appear justified. Given the fortunate rarity of pediatric CSVT, it is possible that future studies will be insufficiently powered to provide a granular analysis of the risks and benefits of anticoagulation in individual groups based on CSVT etiology. Nonetheless, given substantial morbidity and lifestyle restrictions associated with anticoagulation, a measured and individualized approach to treatment in children with transient and treatable causes of CSVT is appropriate, particularly in cases of recent trauma or surgery. We do emphasize the Class I recommendation that if anticoagulation is withheld, repeat neuroimaging, including venous imaging, should be performed in the first week after diagnosis [4]. If thrombus propagation or new infarction or hemorrhage is noted, re-evaluation of the risk-benefit profile of anticoagulation is warranted.

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Declaration of Competing Interest

None. The authors have no disclosures or competing interests.

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