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BRIEF REPORT

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A survey of pediatric hematology/oncology specialists regarding management of central line associated venous thrombosis

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Abstract

Central venous catheters (CVCs) account for the largest proportion of thrombotic events in pediatric patients. Questions remain regarding adequate treatment and prevention methods. We surveyed pediatric hematology/oncology specialists, using hypothetical cases to assess management strategies for acute CVC thrombosis and secondary prevention. Survey respondents varied in the use of the thrombophilia evaluation (33.3%, 41/123) and duration of treatment (6 weeks: 54.1%, 66/122). Secondary CVC prophylaxis was utilized by 36.6% (45/123) of respondents and by 24.4% (30/123) but only if there was a documented thrombophilia. This heterogeneity highlights the need for clinical studies to address these important clinical questions.

KEYWORDS

central venous catheter, pediatric, survey, thrombosis

1 | INTRODUCTION

The presence of a central venous catheter (CVC) is the most significant risk factor for deep vein thrombosis (DVT) in pediatric patients.[1,2] Thrombotic events related to CVCs can lead to significant complications including loss of venous access, pain, swelling, postthrombotic syndrome, and potentially death from a pulmonary embolism. CVC-associated DVT is an increasing pediatric problem and questions remain regarding the most effective way to treat and prevent recurrent CVC-related thrombosis.[3] This case-based survey was designed to assess current management strategies for pediatric patients with a CVC thrombosis with a focus on the use of the thrombophilia evaluation, duration of anticoagulation, and the use of secondary prophylaxis. We hypothesize that there will be significant variation in these three management areas secondary to a current lack of clinical data.

2 | METHODS

A case-based survey was developed by the authors targeting the three management areas of interest including the use of the thrombophilia evaluation, duration of treatment, and the use of secondary prophylaxis. The survey was piloted in the authors' institution and revised based on respondent feedback. The final survey was posted twice (May 27, 2015 and June 10, 2015) on the American Society of Pediatric Hematology/Oncology (ASPHO) clinical forum. The survey included three demographic questions regarding number of

TABLE 1 Respondent demographics

Respondent variable	Total, n = 140 (%)
Type of practice	
Hematology and oncology	119 (85)
Hematology	16 (11.4)
Oncology	5 (3.6)
Years in practice	
Fellow	20 (14.3)
0–5	38 (27.1)
6–10	27 (19.3)
11–15	15 (10.7)
>15	40 (28.6)
Annual number of thrombosis patients at respondent's center	
0–10	20 (14.3)
10–50	73 (52.1)
50–100	33 (23.6)
>100	14 (10)

Abbreviations: ASPHO, American Society of Pediatric Hematology/Oncology; CHEST guidelines, American College of Chest Physicians 9th edition treatment guidelines; CVC, central venous catheter; DVT, deep vein thrombosis

TABLE 2 Case scenario responses

Case 1: A 2-year-old female child is admitted for severe dehydration from viral gastroenteritis. A CVC is placed, and she develops a symptomatic CVC-associated deep vein thrombosis in her right subclavian vein. This is her first thrombotic event and there is no family history of thrombosis.	
Questions	Responses
Would you perform a thrombophilia evaluation?	
Yes	41/123 (33.3%)
No	82/123 (66.7%)
Would you stop anticoagulation at 6 weeks if the ultrasound demonstrates thrombus resolution?	
Yes	66/122 (54.1%)
Yes, but only if the thrombophilia evaluation is normal	16/122 (13.1%)
Yes, but start aspirin	2/122 (1.6%)
No, treat for 12 weeks	38/122 (31.2%)
A year later she is admitted to the intensive care unit with a severe asthma exacerbation requiring placement of a new CVC. Would you place her on anticoagulation to prevent a CVC-associated thrombosis?	
Yes	45/123 (36.6%)
Yes, but only if there was an identified thrombophilia	30/123 (24.4%)
No	48/123 (39%)
If applicable what secondary prophylactic regimen would you use?	
Prophylactic dosing of enoxaparin	66/113 (58.4%)
Therapeutic dosing of enoxaparin	7/113 (6.2%)
Unfractionated heparin prophylactic dosing (10 units/kg/hr)	1/113 (0.9%)
Warfarin (INR goal 1.5–2.5)	1/113 (0.9%)
Aspirin	2/113 (1.7%)
Not applicable	36/113 (31.9%)
Case 2: A 6-year-old female child with standard risk acute lymphoblastic leukemia (B-precursor) just completed 3 months of anticoagulation for a symptomatic CVC-associated clot in the setting of asparaginase therapy during delayed intensification. She is now in the maintenance phase of therapy.	
Questions	Responses
A repeat US demonstrates clot resolution. The same CVC remains in place. Would you continue anticoagulation for the duration of the CVC?	
No	77/119 (64.7%)
If applicable what secondary prophylactic regimen would you use?	
Prophylactic dosing of enoxaparin	35/116 (30.2%)
Therapeutic dosing of enoxaparin	6/116 (5.2%)
Warfarin (INR goal 1.5–2.5 or low dose no INR goal)	3/116 (2.6%)
Aspirin	2/116 (1.7%)
Not applicable	70/116 (60.3%)
What if the initial CVC that resulted in the thrombotic event was removed but she now has a new CVC in place. Would you continue anticoagulation for the new CVC?	
No	87/119 (73.1%)

CVC, central venous catheter.

years in practice, patient population, and annual number of thrombosis patients at the respondent's center. Case scenarios with CVC-associated thrombosis were utilized (Table 2). Case management questions included the use of a thrombophilia evaluation, duration of anticoagulation therapy, and the use of secondary anticoagulation prophylaxis with continued or subsequent CVC placement.

Demographic characteristics were summarized by percentages. Summary statistics for case-based responses were reported using percentages. Proportion of case-based responses were compared using either Fisher's exact test or the χ^2 test separated by respondent factors including total years in practice and annual number of thrombosis patients.

3 | RESULTS

There were a total of 140 responses. The majority (90%, 126/140) were with the first posting. ASPHO reported 1,829 eligible subscribers at the time of posting; we are unable to determine how many actually viewed the posting. Table 1 provides a summary of the respondent's demographics. The case description and responses to management questions are provided in Table 2.

In case 1, a 2-year-old female child with a CVC-associated upper extremity DVT in the setting of an acute illness, 33.3% (41/123) of respondents performed a thrombophilia evaluation; 54.1% (66/122) stopped anticoagulation at 6 weeks after demonstration of clot

resolution without a thrombophilia evaluation, whereas 13.1% (16/122) discontinued at 6 weeks if the thrombophilia evaluation was normal. The patient in case 1 required subsequent CVC placement a year later and 36.6% (45/123) placed her on anticoagulation for secondary prophylaxis, whereas 24.4% (30/123) only used anticoagulation if there was a previously identified thrombophilia.

In case 2, a 6-year-old female child with acute lymphoblastic leukemia with a CVC-associated thrombosis in delayed intensification completed 3 months of anticoagulation with clot resolution but the same CVC remains in place; 64.7% (77/119) of respondents discontinued anticoagulation. If the subject had a new CVC in place, 73.1% (87/119) did not continue anticoagulation.

Responses for each case were analyzed by respondent factors, including total years in practice and annual number of thrombosis patients. No statistical difference was detected in the proportion of responses by each respondent factor.

4 | DISCUSSION

In this survey of pediatric hematologist/oncologists, using specific cases to elicit responses, there was significant variation in the use of the thrombophilia evaluation, duration of treatment for a CVC-associated thrombosis (6 weeks vs. 3 months), and the use of secondary CVC prophylaxis. One-third of respondents sent a thrombophilia evaluation for a patient with a CVC-associated thrombosis. In this clinical setting, debate remains about the utility of thrombophilia testing. The most widely used reference for the management of pediatric thrombosis, the American College of Chest Physicians 9th edition treatment guidelines (CHEST guidelines), comments that the presence or absence of a thrombophilia risk factor should not influence the duration and intensity of treatment.[4] Guidelines from the United Kingdom are more definitive and state that a thrombophilia evaluation is not recommended in patients with a CVC-associated thrombosis.[5] In contrast, our survey demonstrated that not only did one-third of respondents send a thrombophilia evaluation but they used this testing to direct both duration of therapy and whether secondary prophylaxis was indicated for future line placements.

Over half (54%) of respondents stopped anticoagulation after 6 weeks of therapy if there was clot resolution. This is in contrast to the current CHEST guidelines that recommend a treatment duration of 3 months.[4] This recommendation is extrapolated from a randomized clinical trial of 900 adult patients with DVT where DVT recurrence was higher (18.1%) in the 6-week treatment group as compared to the 6-month group (9.5%).[6] Interestingly, a subgroup analysis of this trial demonstrated decreased recurrence rates in those subjects with a provoked DVT.[6] Currently, there are no published studies comparing the duration of anticoagulation in pediatric patients. We await the results of the ongoing KIDS-DOTT study, which is investigating the safety and efficacy of limited treatment duration (6 weeks vs. 3 months) in the setting of a provoked DVT in pediatric patients.[7]

There was a wide variation in the reported use of secondary CVC DVT prophylaxis. For case 2, a 6-year-old female child with acute lymphoblastic leukemia, the majority of respondents (64.7%, 77/119) would not continue anticoagulation after 3 months of therapy even if the same line remained in place. This is despite the CHEST guidelines recommendation to continue anticoagulation, at prophylaxis dosing, if the CVC remains in place after completing the acute DVT treatment course.[4] In contrast, for case 1 when the second CVC was placed in the setting of an acute illness a year after the initial CVC-associated thrombotic event, a higher proportion of respondents (61%) would consider prophylaxis. The 2012 CHEST guidelines recommend against primary prophylaxis after the placement of a central venous line but do not specifically comment on secondary prophylaxis.[4] The lack of high-quality evidence in children leaves clinicians with only clinical judgment and experience to guide their management. There are three randomized clinical trials that studied primary CVC prophylaxis in pediatric patients using prophylactic dosing of either low molecular weight heparin (anti-Xa goal 0.1–0.3), unfractionated heparin (10 units/kg/hr), or warfarin (INR goal 1.3–1.9).[8–10] None of these trials were able to demonstrate a difference in thrombotic events between the two treatment arms, although these studies were generally underpowered. A recent systematic review and meta-analysis of thromboprophylaxis in children was unable to find evidence that thromboprophylaxis reduced the risk of CVC-related thrombosis.[11] Ongoing research is needed to determine the most effective way to prevent both primary and secondary CVC-associated thrombosis.

Limitations of this study include that physicians' self-reporting with a hypothetical situation may differ from their actual management. In addition, as only 140 providers responded to the forum posting, that may represent a biased sample and not fully represent current anticoagulant strategies of all pediatric hematologists/oncologists.

5 | CONCLUSION

This case-based survey demonstrated significant variation in the management of CVC-associated thrombosis and in the use of secondary CVC DVT prophylaxis highlighting the need for ongoing clinical studies to address these important clinical questions.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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