CHILDREN'S ONCOLOGY GROUP

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Guidelines for Management of Venous Thromboembolism: Treatment of Pediatric Venous Thromboembolism

COG Supportive Care Endorsed Guidelines

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The "Guidelines for Management of Venous Thromboembolism: Treatment of Pediatric Venous Thromboembolism" developed by the American Society of Hematology were endorsed by the COG Supportive Care Guideline Committee in May 2019.

The source clinical practice guideline is published (Monagle P, Cuello CA, Augustine C, Bonduel M, Brandao LR, Capman T et al. American Society of Hematology 2018 Guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. Blood Advances 2018; 2 (22): 3293-3316.) and is available at: http://www.bloodadvances.org/content/2/22/3292. Implementation resources provided by the source clinical practice guideline developers may be found at: https://hematology.org/vte/

The purpose of the source clinical practice guideline is to support patients, clinicians, and other health care professionals in their decisions about management of pediatric venous thromboembolism. Recommendations from the endorsed clinical practice guideline are presented in the table below.

Summary of Recommendations for Treatment of Pediatric Venous Thromboembolism

RECOMMENDATIONS	Strength of Recommendation and Certainty in Evidence*
Anticoagulation in symptomatic and asymptomatic deep vein thrombosis (DVT) or pulmonary embolism (PE)	
Should anticoagulation vs no anticoagulation be used in pediatric patients with symptomatic DVT or PE?	
1. The American Society of Hematology (ASH) guideline panel recommends using anticoagulation rather than no anticoagulation in pediatric patients with symptomatic deep vein thrombosis (DVT) or pulmonary embolism (PE)	Strong recommendation Very low certainty in evidence
Should anticoagulation vs no anticoagulation be used in pediatric patients with asymptomatic DVT or PE?	
2. The ASH guideline panel suggests either using anticoagulation or no anticoagulation in pediatric patients with asymptomatic DVT or PE	Conditional recommendation Very low certainty in evidence
Thrombolysis, thrombectomy, and inferior vena cava filters	
Should thrombolysis followed by anticoagulation vs anticoagulation alone be used in pediatric patients with DVT?	
3. The ASH guideline panel suggests against using thrombolysis followed by anticoagulation; rather, anticoagulation alone should be used in pediatric patients with DVT	Conditional recommendation Very low certainty in evidence
Should thrombolysis followed by anticoagulation vs anticoagulation alone be used in pediatric patients with submassive PE?	
4. The ASH guideline panel suggests against using thrombolysis followed by anticoagulation; rather, anticoagulation alone should be used in pediatric patients with submassive PE	Conditional recommendation Very low certainty in evidence

RECOMMENDATIONS	Strength of Recommendation and Certainty in Evidence*
Should thrombolysis followed by anticoagulation vs anticoagulation alone be used in pediatric patients with PE with hemodynamic compromise?	
5. The ASH guideline panel suggests using thrombolysis followed by anticoagulation, rather than anticoagulation alone, in pediatric patients with PE with hemodynamic compromise	Conditional recommendation Very low certainty in evidence
Should thrombectomy followed by anticoagulation vs anticoagulation alone be used in pediatric patients with symptomatic DVT or PE?	
6. The ASH guideline panel suggests against using thrombectomy followed by anticoagulation; rather, anticoagulation alone should be used in pediatric patients with symptomatic DVT or PE	Conditional recommendation Very low certainty in evidence
Should IVC filter vs anticoagulation be used in pediatric patients with symptomatic DVT or PE?	
7. The ASH guideline panel suggests against using inferior vena cava (IVC) filter; rather anticoagulation alone should be used in pediatric patients with symptomatic DVT or PE	Conditional recommendation Very low certainty in evidence
Thrombolysis, thrombectomy, and inferior vena cava filters	
Should antithrombin (AT) replacement in addition to standard anticoagulation vs standard anticoagulation alone be used in pediatric patients with DVT or cerebral sino venous thrombosis (CSVT) or PE?	
8a. The ASH guideline panel suggests against using AT-replacement therapy in addition to standard anticoagulation; rather, standard anticoagulation alone should be used in pediatric patients with DVT/CSVT/PE	Conditional recommendation Very low certainty in evidence
8b. The ASH guideline panel suggests using AT-replacement therapy in addition to standard anticoagulation rather than standard anti-coagulation alone in pediatric patients with DVT/CSVT/PE who have failed to respond clinically to standard anticoagulation treatment and in whom subsequent measurement of AT concentrations reveals low AT levels based on age appropriate reference ranges	Conditional recommendation Very low certainty in evidence
Central venous access device (CVAD)-related thrombosis	
Should removal of a functioning CVAD vs no removal be used in pediatric patients with symptomatic CVAD-related thrombosis who continue to require access?	
9. The ASH guideline panel suggests no removal, rather than removal, of a functioning CVAD in pediatric patients with symptomatic CVAD-related thrombosis who continue to require venous access	Conditional recommendation Very low certainty in evidence
Should removal of a nonfunctioning or unneeded CVADs vs no removal be used in pediatric patients with symptomatic CVAD-related thrombosis?	
10. The ASH guideline panel recommends removal, rather than no removal, of a nonfunctioning or unneeded CVAD in pediatric patients with symptomatic CVAD-related thrombosis	Strong recommendation Very low certainty in evidence

RECOMMENDATIONS	Strength of Recommendation and Certainty in Evidence*
Should immediate removal of a nonfunctioning or unneeded CVAD vs delayed removal be used in pediatric patients with symptomatic CVAD-related thrombosis?	
11. The ASH guideline panel suggests delayed removal of a CVAD until after initiation of anticoagulation (days), rather than immediate removal in pediatric patients with symptomatic central venous line–related thrombosis who no longer require venous access or in whom the CVAD is nonfunctioning	Conditional recommendation Very low certainty in evidence
Should removal of a functioning CVAD vs no removal be used in pediatric patients with symptomatic CVAD-related thrombosis with worsening signs or symptoms, despite anticoagulation, who continue to require access?	
12. The ASH guideline panel suggests either removal or no removal of a functioning CVAD in pediatric patients who have symptomatic CVAD-related thrombosis with worsening signs or symptoms, despite anticoagulation, and who continue to require venous access	Conditional recommendation Very low certainty in evidence
Low-molecular-weight heparin vs vitamin K antagonists	
Should low-molecular-weight heparin vs vitamin K antagonists be used in pediatric patients with symptomatic DVT or PE as maintenance therapy after the first few days?	
13. The ASH guideline panel suggests using either low-molecular weight heparin or vitamin K antagonists in pediatric patients with symptomatic DVT or PE	Conditional recommendation Very low certainty in evidence
Provoked DVT or PE	
Should anticoagulation for > 3 months vs anticoagulation for up to 3 months be used in pediatric patients with provoked DVT or PE?	
14. The ASH guideline panel suggests using anticoagulation for ≤ 3 months rather than anticoagulation for > 3 months in pediatric patients with provoked DVT or PE	Conditional recommendation Very low certainty in evidence
Unprovoked DVT or PE	
Should anticoagulation for > 6 to 12 months vs anticoagulation for 6 to 12 months be used in pediatric patients with unprovoked DVT or PE?	
15. The ASH guideline panel suggests using anticoagulation for 6 to 12 months rather than anticoagulation for > 6 to 12 months in pediatric patients with unprovoked DVT or PE	Conditional recommendation Very low certainty in evidence
CVAD-related superficial vein thrombosis	
Should anticoagulation vs no anticoagulation be used in pediatric patients with CVAD-related superficial vein thrombosis?	
16. The ASH guideline panel suggests using either anticoagulation or no anticoagulation in pediatric patients with CVAD-related superficial vein thrombosis	Conditional recommendation Very low certainty in evidence

RECOMMENDATIONS	Strength of Recommendation and Certainty in Evidence*
Right atrial thrombosis	
Should anticoagulation vs no anticoagulation be used in neonates and pediatric patients with right atrial thrombosis?	
17. The ASH guideline panel suggests using anticoagulation, rather than no anticoagulation, in pediatric patients with right atrial thrombosis	Conditional recommendation Very low certainty in evidence
Should thrombolysis or surgical thrombectomy followed by standard anticoagulation vs anticoagulation alone be used in neonates and pediatric patients with right atrial thrombosis?	
18. The ASH guideline panel suggests against using thrombolysis or surgical thrombectomy, followed by standard anticoagulation; rather, anticoagulation alone should be used in pediatric patients with right atrial thrombosis	Conditional recommendation Very low certainty in evidence
Renal vein thrombosis (RVT)	
Should anticoagulation vs no therapy be used in neonates with RVT?	
19. The ASH guideline panel suggests using anticoagulation, rather than no anticoagulation, in neonates with RVT	Conditional recommendation Very low certainty in evidence
Should thrombolysis followed by standard anticoagulation vs anticoagulation alone be used in neonates with RVT (life-threatening or nonlife-threatening)?	
20a. The ASH guideline panel recommends against using thrombolysis, followed by standard anticoagulation; rather, anti-coagulation alone should be used in neonates with nonlife-threatening RVT	Strong recommendation Very low certainty in evidence
20b. The ASH guideline panel suggests using thrombolysis followed by standard anticoagulation rather than anticoagulation alone in neonates with life-threatening RVT	Conditional recommendation Very low certainty in evidence
Portal vein thrombosis (PVT)	
Should anticoagulation vs no anticoagulation be used in pediatric patients with PVT?	
21a. The ASH guideline panel suggests using anticoagulation, rather than no anticoagulation, in pediatric patients with PVT with occlusive thrombus, postliver transplant, and idiopathic PVT	Conditional recommendation Very low certainty in evidence
21b. The ASH guideline panel suggests using no anticoagulation, rather than anticoagulation, in pediatric patients with PVT with nonocclusive thrombus or portal hypertension	Conditional recommendation Very low certainty in evidence

RECOMMENDATIONS	Strength of Recommendation and Certainty in Evidence*
Cerebral sino venous thrombosis (CVST)	
Should anticoagulation vs no anticoagulation be used in pediatric patients with CSVT?	
22a. The ASH guideline panel recommends using anticoagulation, rather than no anticoagulation, in pediatric patients with CSVT without hemorrhage	Strong recommendation Very low certainty in evidence
22b. The ASH guideline panel suggests using anticoagulation, rather than no anticoagulation, in pediatric patients with CSVT with hemorrhage	Conditional recommendation Very low certainty in evidence
Should thrombolysis followed by standard anticoagulation vs anticoagulation alone be used in pediatric patients with CSVT?	
23. The ASH guideline panel suggests against using thrombolysis followed by standard anticoagulation; rather, anticoagulation alone should be used in pediatric patients with CSVT	Conditional recommendation Very low certainty in evidence
Purpura fulminans due to homozygous protein C deficiency	
Should protein C replacement vs anticoagulation be used in pediatric patients with congenital purpura fulminans due to homozygous protein C deficiency?	
24. The ASH guideline panel suggests using protein C replacement, rather than anticoagulation, in pediatric patients with congenital purpura fulminans due to homozygous protein C deficiency	Conditional recommendation Very low certainty in evidence
Should anticoagulation plus protein C replacement vs anticoagulation alone be used in pediatric patients with congenital purpura fulminans due to homozygous protein C deficiency?	
25. The ASH guideline panel suggests using anticoagulation plus protein C replacement, rather than anticoagulation alone, in pediatric patients with congenital purpura fulminans due to homozygous protein C deficiency	Conditional recommendation Very low certainty in evidence
Should liver transplantation vs no liver transplantation (anticoagulation or protein C replacement) be used in pediatric patients with congenital purpura fulminans due to homozygous protein C deficiency?	
26. The ASH guideline panel suggests using either liver transplantation or no liver transplantation (anticoagulation or protein C replacement) in pediatric patients with congenital purpura fulminans due to homozygous protein C deficiency	Conditional recommendation Very low certainty in evidence

*see Appendix 1

Appendix 1: GRADE

Strength of Recommendations:

Strong Recommendation	When using GRADE, panels make strong recommendations when they are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.
Weak or Conditional Recommendation	Weak or conditional recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Strength of Recommendation Determinants:

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Certainty in evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted

Certainty in Evidence or Quality of Evidence

High Certainty/Quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate Certainty/Quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low Certainty/Quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low Certainty/Quality	Any estimate of effect is very uncertain

Guyatt, G.H., et al., *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations.* BMJ, 2008; 336: 924-926.
Guyatt, G.H., et al., *GRADE: going from evidence to recommendations.* BMJ, 2008; 336: 1049-1051.