CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

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Antithrombotic Therapy in Neonates and Children: Antithrombotic Therapy and Prevention of Thrombosis

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The "Antithrombotic Therapy in Neonates and Children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-based Clinical Practice Guidelines" were endorsed by the COG Supportive Care Guideline Committee in May 2015. The entire document and is available at: http://journal.publications.chestnet.org/article.aspx?articleID=1159589
Supplementary material provided by the guideline developers is available at:
http://chestjournal.chestpubs.org/content/suppl/2012/02/03/141.2_suppl

The purpose of this guideline is to provide evidence-based recommendations for antithrombotic therapy in neonates and children with cancer and the perioperative management of antithrombotic therapy.

The recommendations of the endorsed guideline pertaining to children receiving cancer treatment are provided here.

I. Summary of Recommendations for Antithrombotic Therapy in Neonates and Children with Cancer

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
GENERAL MANAGEMENT OF PEDIATRIC PATIENTS WITH THROMBOEMBOLISM	
Pediatric patients with thromboembolism:	
• Suggest that where possible, pediatric hematologists with experience in thromboembolism manage pediatric patients with thromboembolism	Weak recommendation, low- or very-low-quality evidence
• When this is not possible, suggest a combination of a neonatologist/pediatrician and adult hematologist supported by consultation with an experienced pediatric hematologist	Weak recommendation, low- or very-low-quality evidence
VTE IN CHILDREN	
Children with first VTE (CVAD and non-CVAD related)	
• Recommend acute anticoagulation therapy with either UFH or LMWH	Strong recommendation, moderate-quality evidence
• Recommend initial treatment with UFH or LMWH for at least 5 days	Strong recommendation, moderate-quality evidence
• For ongoing therapy, recommend LMWH	-
Children with secondary VTE (ie VTE that has occurred association with a clinical risk factor) whom the risk factor has resolved:	
• Suggest continuing anticoagulant therapy beyond 3 months as compared with no further therapy	Weak recommendation, low- or very-low-quality evidence
Children who have ongoing but potentially reversible risk factors such as active nephrotic syndrome or ongoing asparaginase therapy:	
• Suggest continuing anticoagulant therapy beyond 3 months in either therapeutic or prophylactic doses until the risk factor has resolved	Weak recommendation, low- or very-low-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
Children with a CVAD place who have a VTE:	
• If a CVAD is no longer required or is nonfunctioning, recommend it be removed	Strong recommendation, moderate-quality evidence
• Suggest at least 3 to 5 days of anticoagulation therapy prior to its removal rather than no anticoagulation prior to removal	Weak recommendation, low- or very-low-quality evidence
• If CVAD access is required and the CVAD is still functioning, suggest that the CVAD remain in situ and the patient given anticoagulants	Weak recommendation, low- or very-low-quality evidence
Children with first CVAD-related VTE:	
• Suggest initial management as for secondary VTE as previously described	-
Children with CVAD in place who a VTE and in whom the CVAD remains necessary:	
• Suggest, after the initial 3 months of therapy, that prophylactic doses of VKAs (INR range, 1.5-1.9) or LMWH (anti-Xa level range, 0.1-0.3 units/mL) be given until the CVAD is removed	Weak recommendation, low- or very-low-quality evidence
• If recurrent thrombosis occurs while the patient is receiving prophylactic therapy, suggest continuing therapeutic doses until the CVAD is removed and for a minimum of 3 months following the VTE	Weak recommendation, low- or very-low-quality evidence
DVT IN CHILDREN WITH CANCER	
Children with cancer:	
• Suggest that management of VTE follow the general recommendations for management of VTE in children	-
• Suggest the use of LMWH in the treatment of VTE for a minimum of 3 months until the precipitating factor has resolved (eg, use of asparaginase) *Remarks: The presence of cancer, the need for surgery, chemotherapy, or other treatments may modify the risk-benefit ratio for treatment of VTE, and clinicians should consider these factors on an individual basis*	Weak recommendation, low- or very-low-quality evidence
CHILDREN WITH CVADS	
Children with CVADs:	
• Suggest flushing with normal saline or heparin or intermittent recombinant urokinase to maintain patency as compared with no therapy	Weak recommendation, low- or very-low-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
Children with blocked CVADs:	
• Suggest tPA or recombinant urokinase to restore patency	Weak recommendation, low- or very-low-quality evidence
• If at least 30 minutes following local thrombolytic instillation CVAD patency is not restored, suggest a second dose be administered	-
• If the CVAD remains blocked following two doses of local thrombolytic agent, suggest radiologic imaging to rule out a CVAD-related thrombosis	Weak recommendation, low- or very-low-quality evidence
Children with short- to medium-term CVADs:	
• Recommend against the use of routine systemic thromboprophylaxis	Strong recommendation, moderate-quality evidence

II. Summary of Recommendations for Perioperative Management of Antithrombotic Therapy

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
PERIOPERATIVE USE OF IV UFH	
Patients who are receiving bridging anticoagulation with therapeutic-dose IV UFH:	
• Suggest stopping UFH 4 to 6 h before surgery instead of closer to surgery	Weak recommendation, low- or very-low-quality evidence
PERIOPERATIVE INTERRUPTION OF THERAPEUTIC-DOSE BRIDGING LMWH	
Patients who are receiving bridging anticoagulation with therapeutic-dose SC LMWH:	
• Suggest administering the last preoperative dose of LMWH approximately 24 h before surgery instead of 12 h before surgery	Weak recommendation, low- or very-low-quality evidence
POSTOPERATIVE RESUMPTION OF THERAPEUTIC-DOSE BRIDGING LMWH	
Patients who are receiving bridging anticoagulation with therapeutic-dose SC LMWH and are undergoing high-bleeding-risk surgery:	
• Suggest resuming therapeutic dose LMWH 48 to 72 h after surgery instead of resuming LMWH within 24 h after surgery	Weak recommendation, low- or very-low-quality evidence

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 Recommendation	Weak recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Strength of Recommendations 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
Quality of 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

Quality of Evidence

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