Commentary: Thromboprophylaxis after congenital cardiac surgery—Time for evidence-based guidelines

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In the current issue of the *Journal*, Vorisek and colleagues¹ report the results of a single-center retrospective study of postoperative anticoagulation with unfractionated heparin (UFH) in 966 consecutive pediatric cardiac surgical cases. Their aim was to identify heparin doses that prevent thrombosis but do not increase bleeding. Subjects were stratified as those treated with no UFH, low-dose UFH (<15 U/kg/h), and high-dose (>15 U/kg/h). Nearly two-thirds of subjects received UFH postoperatively, and most also received antiplatelet therapy. The data were analyzed with multivariable logistic regression as well as propensity score analysis to identify the risk of bleeding or thrombosis among groups. Vorisek and colleagues¹ concluded that high-dose UFH was associated with significantly more bleeding and thrombosis.

After pediatric cardiopulmonary bypass, bleeding and thrombosis remain major sources of morbidity and mortality. Risk factors include young age, small size, single-ventricle palliation, use of deep hypothermia, and high surgical complexity.^{2,3} Postthrombotic mortality rates may exceed 25% in high-risk cohorts.³ When evaluating the demographics within the study by Vorisek and colleagues,¹ it is important to note a significantly greater proportion of at-risk subjects were found within the high-dose UFH cohort. In addition, Vorisek and colleagues¹ observed a high rate of bleeding with a relatively low rate of thrombosis, which raises the question of whether high-dose UFH may have actually conferred an antithrombotic benefit.

Because of the retrospective nature of the review, the intended level of anticoagulation could not be definitively determined, and laboratory monitoring of heparinization could not be provided. This is critical after pediatric cardiac surgery, when patient-related (developmental hemostasis, cyanosis) and bypass-related (hemodilution, consumption, inflammation) pathophysiology create variability in heparin dose response. When therapeutic anticoagulation is desired, activated partial thromboplastin time (aPTT) and

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Central Message

This study identifies potential complications related to high-dose heparin after pediatric cardiac surgery. High-quality prospective studies are needed to develop risk-stratified thromboprophylaxis guidelines.

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anti-factor Xa levels are commonplace for heparin dose titration. These tests are not without shortcomings, however, because significant discordance may exist between aPTT and anti-factor Xa levels. Developmental hemostasis and factor depletion affect the intrinsic pathway-dependent aPTT, whereas antithrombin 3 levels affect anti-Xa activity. Important work by Oladunjoye and associates⁴ has shown that aPTT levels greater than 150 seconds are associated with increased bleeding after congenital cardiac surgery, whereas anti-Xa levels do not predict bleeding events. This discordance between aPTT and anti-Xa levels inspired the development of an UFH dose titration protocol that was based on both assay; this resulted in reduced clinically relevant bleeding and time spent with supratherapeutic heparin levels.⁵

Vorisek and colleagues¹ are to be commended for studying outcomes associated with varying UFH doses. This highly relevant topic is of great consequence to our patients and has not been adequately addressed in the existing literature. Many questions, however, remain unanswered. Ultimately, high-quality prospective, randomized studies that incorporate laboratory monitoring are essential to provide risk-stratified, evidence-based thromboprophylaxis guidelines for pediatric cardiac surgical patients.

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