Goldilocks meets heparin dosing—enough but not too much

Jonathan R. Egan, MBBS, PhD, FRACP, FCICM,^{a,d} Tatjana Kilo, FRCPA,^b and David S. Winlaw, MBBS, MD, FRACS^{c,d}

From the ^aPaediatric Intensive Care, ^bDepartment of Haematology, and ^cHeart Centre for Children, The Children's Hospital at Westmead, Sydney, New South Wales, Australia; and ^dSchool of Child and Adolescent Health, University of Sydney, Sydney, New South Wales, Australia.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication March 2, 2018; accepted for publication March 7, 2018; available ahead of print April 10, 2018.

Address for reprints: David S. Winlaw, MBBS, MD, FRACS, Heart Centre for Children, The Children's Hospital at Westmead, Westmead, New South Wales 2145, Australia (E-mail: david.winlaw@sydney.edu.au).

J Thorac Cardiovasc Surg 2018;156:341-2

0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2018.03.041>

Sometimes the status quo is so deeply embedded, it is difficult to change practice without compelling evidence. In monitoring of anticoagulation, the superiority of anti-Xa levels over activated partial thromboplastin time (aPTT) is routinely advised. A more nuanced picture is provided by Oladunjoye and colleagues¹ within the frame of postoperative cardiac care, emphasizing the role of aPTT in defining the risk of bleeding complications. Compelling? Yes.

A lack of correlation between APTT and anti-Xa in monitoring heparin levels has been shown in several pediatric studies,² most elegantly by Newall and colleagues³ in a series of patients who received cardiac catheterization. Further, in a study of 39 patients, it was demonstrated that discordance between high aPTT and therapeutic range anti-Xa levels was associated with major bleeding events.⁴ Similar findings have been observed in adults, with the same pattern of discordance also found to be associated with worse outcomes. In a study of more than 500 patients, it was found that aPTT and anti-Xa levels were frequently discordant, with prolonged aPTT relative to anti-Xa the most common finding. This cohort had increased risks of significant bleeding and higher 30-day mortality.⁵ Consequently, it was suggested to pragmatically use anti-Xa levels to provide an estimate of heparin concentration, whereas aPTT informed the background coagulation status and potential risk/benefit of anticoagulation. However, no specific algorithm was suggested, just that high aPTT, relative to anti-Xa, was an important risk.

Oladunjoye and colleagues¹ proposed a guideline on the basis of their experience in a year-long single-center review of heparinized postoperative infants and children. It was found that important bleeding events were similarly associated with high aPTT levels and concurrently measured normal-range anti-Xa levels. This finding led to a change in practice in which heparin dosing was not escalated on the basis of anti-Xa levels if the aPTT exceeded

David S. Winlaw, MBBS, MD, FRACS, and Jonathan R. Egan, MBBS, PhD, FRACP, FCICM

Central Message

Prevention of bleeding complications of heparin therapy requires measurement of aPTT and anti-Xa. The rationale for heparin therapy and its efficacy in prevention of thrombosis require further work.

See Article page 332.

100 seconds. The algorithm is a pragmatic approach to heparin use in this patient group, noting that there was no routine surveillance for thrombosis and patients receiving extracorporeal life support were not included.

This work will improve the safety of heparin therapy but raises other questions about commonly accepted practices. We are left wondering what measure best defines the lower limit of effective anticoagulation and whether “effective” anticoagulation actually prevents thrombosis in our patients. Neonates with intra-atrial lines after Norwood surgery are at particular risk of thromboembolism, and sometimes thrombus forms despite adequate anticoagulation.⁶ Other practices, such as heparinizing patients after Fontan completion, also could be reconsidered, with diverse approaches seemingly yielding similar outcomes.

The original work describing use of aPTT and anti-Xa levels in the monitoring of anticoagulation stems from a report in 1972.⁷ Increased sophistication in this field will involve routine surveillance of thrombus, concurrent measurement of antithrombin III levels, and assessment of the dynamic contribution of dynamic clot formation with thromboelastography. It is understood that titration of heparin will never be a precise science. For now, this study provides 2 important practice pointers: Routinely measure both

aPTT and anti-Xa, and do not escalate heparin dosing if the aPTT is 100 seconds or more.

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