Searching for an Alternate Anticoagulant for Cardiopulmonary Bypass: Does Two Plus Two Equal Two?

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GLOSSARY

ACT = activated clotting time; **AT** = antithrombin; **CPB** = cardiopulmonary bypass; **DTI** = direct thrombin inhibitor; **HIT** = heparin induced thrombocytopenia; **INR** = international normalized ratio; **UFH** = unfractionated heparin; **Va** = activated Factor V; **X** = Factor X; **Xa** = activated Factor X

Unfractionated heparin (hereinafter heparin) has been the mainstay anticoagulant used during cardiopulmonary bypass (CPB) for >6 decades. Its dominance persists despite the limitations of requiring a cofactor (antithrombin), having a variable response in any given individual (hence the need for frequent monitoring) and potentially causing a life- and limb-threatening disease (heparin-induced thrombocytopenia [HIT]). It is notable that the anticoagulant used for the first successful use

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amount of brin deposition on the arterial lters was once again consistent with that found using 3 u/mL of heparin. Although theoretically possible, reversal of the rivaroxaban with andexanet alpha was not tested in combination with idarucizumab to reverse the effects of the dabigatran.

So can 2 pairs of anticoagulant-antidote combinations do the job of a heparin-protamine duo? It is important to note that a parenteral DTI for CPB anticoagulation already exists. Bivalirudin has been successfully utilized for CPB anticoagulation for more than a decade and a half, albeit with some drawbacks.[9] It is well known that its relatively short 20- to 30-minute elimination half-life can increase by a factor of 5 or more in renally compromised patients, and it of course lacks an antidote.[10] Less appreciated is the fact that bivalirudin inhibits thrombin reversibly, making it less effective at preventing clot propagation and cre-

test, the rapidTEG clotting time, or R-time, averaged 40 to 50 minutes to produce a result.[2] This would signi cantly limit its value as a point-of-care test. Even if the test could be accelerated, it is sometimes dif - cult to predict the effects of a particular drug on the assay. Dabigatran, like coumadin, generally has a synergistic effect with heparin on the ACT, but Factor Xa inhibitors can have a "blunting" effect, causing the ACT to increase more gradually for any given heparin amount.[15] Using 2 anticoagulants would necessitate understanding how each agent affected the test result so they could be effectively titrated. Clearly, this is an area in need of further research.

If heparin is to be replaced for CPB anticoagulation, it will de nitely require some out-of-the-box thinking. While there are clearly multiple hurdles to a dabigatran and rivaroxaban regimen, we applaud Nadtochiy et al for demonstrating some creativity. Unlike ancrod, at least the required reversal agents are already in existence.

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