thrombus formation continues to be a problem in these patients despite use of dual antiplatelet therapy.^{2,5} Although transcatheter valves were explicitly excluded from the present study,¹ a well-designed and thoughtful trial considering the use of NOAC versus warfarin in patients following transcatheter valve implantation is perhaps warranted.

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See Article page 58.

Commentary: Battle of the bioprosthetic valve blood thinners

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Shim and colleagues¹ present a prospective, nonblinded, randomized control trial of 218 patients who either received edoxaban or warfarin following surgical bioprosthetic valve replacement or valve repair. Their results are impressive, and more importantly, because there is an unmet clinical need for an alternative to warfarin, their message of edoxaban's noninferiority is timely and essential.

Warfarin inhibits the production of several coagulation factors. Despite its narrow therapeutic window, dietary interactions, and adherence issues, it has long been the only option for long-term oral anticoagulation. Additionally, some patients may be genetically hyper- or hyporesponsive to warfarin, which poses difficulties in the postoperative management. On the other hand, promising alternatives to

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CENTRAL MESSAGE

The clinical significance of postoperative thrombotic events necessitates choosing the optimal blood thinners in patients undergoing valvular surgery to improve cardiac surgery care and outcomes.

warfarin such as direct oral anticoagulants—inhibit activated factor X—have shown noninferiority and significantly less bleeding compared with warfarin.² Furthermore, they have shown superiority in preventing stroke and systemic embolism.³ However, they are still limited in their use for nonvalvular atrial fibrillation.

The optimal anticoagulation therapy following valvular surgery is still a matter of debate due to limited evidence.⁴ An appealing rationale for perioperative anticoagulation includes minimizing thrombus formation on the bioprosthetic valve and suture material that has not undergone

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endothelialization. In a study of the national Adult Cardiac Surgery Database, Schwann and colleagues⁵ found substantial surgeon and hospital variability in following the suggested guidelines, with more than 50% of patients receiving warfarin as their anticoagulation therapy. Many surgeons still discharge patients on aspirin alone, favoring antiplatelet therapy over other anticoagulation therapies, especially following mitral valve repair. In patients with bioprosthetic valves, the authors found that edoxaban was noninferior to warfarin with respect to death, thromboembolic events, or intracardiac thrombosis. Patients given edoxaban had less clinically relevant nonmajor bleeding and rehospitalization 90 days postoperatively. The results were consistent among subgroups of patients with atrial fibrillation, different types of valve surgery, or concomitant surgery. But contrary to previous literature showing apixaban superiority to warfarin with respect to bleeding,³ the results of the present study indicate that edoxaban could be different than other direct oral anticoagulants, where there is a slight increase of bleeding risk of more than 5% over warfarin.

This study is potentially a practice-changing critical trial. Despite the compelling results, the robustness of these studies is confined by the small number of patients and events in each group, suggesting caution in its real-world applicability. However, edoxaban provides a first glimpse into alternative therapy in the early period after bioprosthetic valve replacement. Similar results were observed

in a subgroup analysis of the Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48 (ENGAGE AF-48) trial in 191 patients with bioprosthetic valves.⁶ Given the wide noninferiority margins and the few events observed in both groups in the present study, a proper study of alternative therapies is clearly warranted in a large-scale randomized controlled multicenter clinical trial. Concomitantly, in patients with bioprosthetic valves and valve repair, other therapies should be included in comparison studies, such as aspirin alone versus other anticoagulant agents.

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