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Commentary: Do you DOAC? Direct oral anticoagulants in patients with bioprosthetic valves

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Over the last decade, direct oral anticoagulants (DOACs) have become increasingly common in clinical practice as an alternative to vitamin K antagonists (VKAs), such as warfarin. The lack of need for routine monitoring, serum levels largely independent of diet, and fewer medication interactions add to their preference over VKAs for many patients and prescribers. Despite a robust literature supporting their safety and efficacy overall, data relevant to patients with bioprosthetic valves remain limited.

In this issue of the *Journal*, Yokoyama and colleagues¹ report a meta-analysis comparing outcomes of patients with bioprosthetic valves treated with DOACs or VKAs for atrial fibrillation. In total, they included 10 studies (4 randomized controlled trials and 6 observational studies) with more than 6000 patients. Pooled data from the analysis demonstrated similar rates of all-cause death and the combined end point of stroke or systemic embolism, whereas major bleeding was lower with a hazard ratio of 0.66. The authors appropriately discuss the limitations inherent to their analysis in that 4 different DOACs were combined into 1 treatment group and several different valve positions and implantation techniques were included. The authors should be commended on their effort and the addition to the literature; however, given these limitations, conclusion from this study should not be considered definitive.

Guidelines from Europe² recognize that anticoagulant selection in patients with atrial fibrillation and bioprosthetic

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CENTRAL MESSAGE

There is a growing body of literature supporting the use of DOACs for atrial fibrillation thromboembolism prophylaxis in patients with bioprosthetic valves.

valves is a grey area but do endorse DOACs in this setting as “a valid option” (with the caveat of being at least 3 months from valve replacement). The more recent 2020 American guidelines³ give an even stronger recommendation, now endorsing DOACs in this population with a class IA recommendation. Future iterations of the guidelines will sustain and perhaps extend this recommendation with the publication of the RIVER trial,⁴ a prospective randomized trial demonstrating noninferiority of rivoraxaban for thromboembolism prophylaxis in patients with atrial fibrillation and a bioprosthetic mitral valve. This landmark study was unique in that it specifically included a targeted cohort rather than relying on post hoc analyses as had been reported. The RIVER trial was included in the present meta-analysis and served as the source of most patients from the 4 randomized trials.

This report is a welcome addition, expanding data in support of DOACs in the cardiac surgical population, both in the perioperative period and for those with previously implanted bioprosthetic valves. The enthusiasm for their use after cardiac surgery has rapidly increased, perhaps outpacing data specific to this population. Our group, using a state-wide database, found that the percentage of patients prescribed DOACs after cardiac surgery more than tripled in a 7-year study period, increases that were most pronounced in patients with bioprosthetic valves (increases of 2.2%/year and 2.7%/year for aortic valve and mitral valve

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replacements, respectively).⁵ In contrast, prospective randomized data for the use of DOACs in patients with atrial fibrillation and a bioprosthetic valve has only been available in the last year.

The use of DOACs in patients with bioprosthetic valves will continue to increase. The question remains: Is there enough evidence to definitively recommend these agents in routine practice? More data will continue to emerge, including from the NEW-AF study (NCT03702582), which aims to complete enrollment in 2023. Although the study is primarily evaluating anticoagulation strategies for new-onset atrial fibrillation, patients with bioprosthetic valves are included and should add to our understanding of DOACs early after bioprosthetic valve replacement, an area that is lacking. In general, the presence of a bioprosthetic valve probably should not impact anticoagulant selection in patients with atrial fibrillation that is unrelated to rheumatic disease. However, until more data become available, the decision to use this class of medications early after cardiac

surgery should be made with an understanding of the current evidence and ideally in the context of clinical trials.

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