See Article page 71.

Commentary: Direct oral anticoagulants in heart surgery: A question in need of an answer

Stephen D. Waterford, MD, MS,^a and Niv Ad, MD^b

Stephen D. Waterford, MD, MS, and Niv Ad, MD

The Invited Expert Opinion by Drs Kapadia and Svensson¹ is focused on an important clinical challenge of whether direct oral anticoagulants (DOACs) can be used in patients with bioprosthetic valves who have atrial fibrillation (AF). Recommendations for anticoagulation therapy should focus on potential risks of early postoperative bleeding with DOAC treatment and not only on its long-term superiority over vitamin K antagonists (VKAs) for stroke prevention in patients with AF, with or without a bioprosthetic valve. The authors focused on the RIVER trial, which compared rivaroxaban with warfarin in patients with AF and a bioprosthetic mitral valve.² This trial showed a significant decrease in stroke in the rivaroxaban group at 1 year and a trend of reduced risk of death from cardiovascular or thromboembolic causes and reduced risk of bleeding. In this trial, rivaroxaban showed no statistically significant difference in bioprosthetic leaflet thrombosis compared with VKAs.

There are several points that should be considered while reading this Expert Opinion:

1. The RIVER trial findings are altogether expected, but important. Because DOACs have been found superior to VKAs for patients with AF without a bioprosthesis, it may not be surprising that they remain superior in patients with AF and bioprosthetic valves.
2. The larger issue to address from the RIVER trial is as follows: If DOACs are superior to VKAs in patients with a bioprosthetic mitral valve, can they be started

CENTRAL MESSAGE

Large-scale randomized trials of DOACs and VKAs immediately after cardiac surgery are needed to understand which class of medications has better benefit in real-world practice.

immediately after the mitral valve replacement itself? This question is the subject of our recent review in the *Journal*³ and highlights the need for a high-quality randomized controlled trial of DOACs after cardiac surgery to establish the safety of such treatment. Such a trial would enroll patients with new-onset postoperative AF and patients with a bioprosthetic valve replacement and would randomize them to receive a DOAC or VKA during the same hospitalization. The primary end point would be bleeding events at 30 and 90 days. Thromboembolic events would also be collected, but all currently available evidence indicates a lower rate of thromboembolic events with DOACs versus VKAs. We agree with the general sentiment of the article that DOACs would serve patients better long-term, but we want to highlight the need to establish the safety of DOACs early after cardiac surgery. This question remains unanswered because more than 80% of patients in the RIVER trial were enrolled more than 3 months after mitral valve replacement. Indeed, if DOACs could be demonstrated as safer and more effective than VKAs immediately after cardiac surgery, then there would be no reason to select a VKA other than a contraindication to DOAC.

3. With respect to transcatheter aortic valve replacement (TAVR), although the GALILEO trial⁴ referenced by Drs Kapadia and Svensson¹ showed higher adverse events in the rivaroxaban plus aspirin group compared with the dual antiplatelet therapy group, it is important to consider that patients in the trial did not have an

From the ^aDivision of Cardiac Surgery, Department of Surgery, SUNY Upstate Medical University, Syracuse, NY; and ^bDivision of Cardiac Surgery, Department of Surgery, Adventist HealthCare, Silver Spring, Md.

Disclosures: The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication June 7, 2021; revisions received June 7, 2021; accepted for publication June 7, 2021; available ahead of print June 11, 2021.

Address for reprints: Niv Ad, MD, Division of Cardiac Surgery, University of Maryland School of Medicine, 110 S. Paca St, 7th Floor, Baltimore, MD 21201 (E-mail: nivadmd14@gmail.com).

J Thorac Cardiovasc Surg 2023;165:76-7

0022-5223/\$36.00

Copyright © 2021 by The American Association for Thoracic Surgery

<https://doi.org/10.1016/j.jtcvs.2021.06.013>

established indication for anticoagulation after TAVR, such as AF, and anticoagulation is controversial in this group. The multicenter ATLAS trial, published in 2020, examined patients who underwent TAVR but also had an indication for oral anticoagulation and compared those who received a DOAC with those who received a VKA in a nonrandomized retrospective review.⁵ Within the limits of this nonrandomized review, there was no difference in 30-day mortality or in-hospital major or life-threatening bleeding between DOACs and VKAs. The persistent uncertainty surrounding DOACs after TAVR is reflected in the current American Heart Association/American College of Cardiology Guidelines, which state that use of VKAs after TAVR in patients with coexisting indication for long-term anticoagulation has a IIb level of recommendation.⁶ This reflects the need for a randomized trial of DOACs versus VKAs after TAVR, starting with patients who do have a coexisting indication for long-term anticoagulation.

As cardiac surgeons, we understand the difference in mechanisms between DOACs and VKAs. DOACs have immediate onset of anticoagulation, which is the reason why many surgeons do not use them early after surgery. However, they do not require monitoring and have fewer dietary restrictions, leading to patients who are more likely to be properly anticoagulated and less likely to bleed, at least when used outside the immediate postoperative setting. It

is only through a large-scale randomized trial of DOACs and VKAs immediately after cardiac surgery that we will understand which class of medications has better benefit in real-world practice. Cardiac surgeons should also remember that patients with AF should be treated with appropriate surgical ablation whenever possible and that there is a clear benefit in these patients to excluding the left atrial appendage (LAAOS III trial).⁷

References

1. Kapadia SR, Svensson LG. Bioprosthetic valves and atrial fibrillation: direct anticoagulants or warfarin. *J Thorac Cardiovasc Surg.* 2023;165:71-5.
2. Guimaraes HP, Lopes RD, de Barros E Silva PGM, Liporace IL, Sampaio RO, Tarasoutchi F, et al. Rivaroxaban in patients with atrial fibrillation and a bioprosthetic mitral valve. *N Engl J Med.* 2020;383:2117-26.
3. Dangas GD, Tijssen JGP, Wohrle J, Sondergaard L, Gilard M, Mollmann H, et al. A controlled trial of rivaroxaban after transcatheter aortic valve replacement. *N Engl J Med.* 2020;382:120-9.
4. Waterford SD, Ad N. Nonvitamin K oral anticoagulants in cardiac surgery: what cardiothoracic surgeons need to know 2.0. *J Thorac Cardiovasc Surg.* March 19, 2021 [Epub ahead of print].
5. Kalogeras K, Jabbour RJ, Ruparelia N, Watson S, Kabir T, Naganuma T, et al. Comparison of warfarin versus DOACs in patients with concomitant indication for oral anticoagulation undergoing TAVI: results from the ATLAS registry. *J Thromb Thrombolysis.* 2020;50:82-9.
6. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. *Circulation.* 2019;140:e125-41.
7. Whitlock RP, Belley-Cote EP, Paparella D, Healey JS, Brady K, Sharma M, et al. Left atrial appendage occlusion during cardiac surgery to prevent stroke. *N Engl J Med.* 2021;384:2081-91.