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EDITORIAL COMMENT

The balance between thrombosis and bleeding after mitral valve surgery: The need for robust evidence

Equilíbrio trombótico/hemorragia após cirurgia da válvula mitral: necessidade de provas sólidas

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The optimal strategy for oral anticoagulation (OAC) in patients after surgical mitral valve repair (MVR) or mitral bioprosthetic valve replacement (BVR) remains a contentious issue within the cardiovascular community, especially during the early postoperative period.

The European Society of Cardiology (ESC) provides specific guidelines for anticoagulation in these patients.[1] For mechanical mitral valve replacement, lifelong anticoagulation with vitamin K antagonists (VKAs) is recommended due to the high risk of thromboembolic events. By contrast, for bioprosthetic valves, VKAs are recommended for the first three months following surgery, after which switching to antiplatelet therapy may be considered if there are no other indications for anticoagulation. Non-vitamin K antagonist oral anticoagulants (NOACs) are contraindicated in mechanical valve patients and are only cautiously recommended for those with bioprosthetic valves after the initial high-risk period (class of recommendation IIb, level of evidence C). These guidelines reflect ongoing uncertainty and the need for more evidence on the safety and efficacy of NOACs in these settings.

Despite the guidelines, the off-label use of NOACs in the first three months post-surgery has been increasing, as highlighted in an article published in 2020.[2] A recent systematic review and meta-analysis of randomized controlled trials comparing NOACs to VKAs in the first 90 days after bioprosthetic valve implantation found no difference with regard to thrombosis, bleeding or death.[3] However, there is still an unmet need for robust evidence to either support or reject this practice.

In the current issue of the *Journal*, Costa et al.[4] set out to compare NOACs to VKAs in terms of efficacy and safety during the first three months following MVR or mitral BVR. While the findings suggest a potential advantage for NOACs, a critical assessment is necessary to understand the study's methodology, results, and broader implications.

The study[4] used a single-center retrospective analysis with prospectively collected data from patients treated between 2020 and 2021. Retrospective studies, although useful for real-world insights, are inherently limited by biases, including selection bias, and unmeasured confounding variables. The absence of randomization in assigning patients to VKAs or NOACs introduces potential biases that could skew the results.

Patients were divided into two groups based on the OAC strategy at discharge: VKAs or NOACs. The primary outcome was a composite of death, rehospitalization, myocardial infarction, stroke or transient ischemic attack, systemic embolism, mitral thrombosis, or bleeding within three months of surgery. This broad outcome measure, while comprehensive, could obscure the specific risks and benefits associated with each anticoagulant type.

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At discharge, 66.2% of patients were prescribed VKAs, while 33.8% received NOACs. The primary outcome occurred significantly less frequently in the NOAC group (6%) than in the VKA group (22.4%), primarily due to a higher incidence of bleeding events in the VKA group (p=0.012). Smoking and VKA use were identified as independent predictors of adverse outcomes.

While these findings are compelling, the retrospective design and single-center scope of the study limit their generalizability. The criteria for selecting NOACs versus VKAs are not detailed, potentially introducing bias.

The study suggests that NOACs may offer a safer profile than VKAs in the early postoperative period, mainly due to fewer bleeding events. However, the study's retrospective nature and lack of randomization could potentially lead to selection bias, with patients prescribed NOACs possibly having a lower inherent risk profile.

The three-month follow-up period is valuable for capturing immediate postoperative outcomes but insufficient for assessing long-term safety and efficacy. It remains unclear whether the early benefits observed with NOACs are sustained over time and whether late complications could alter the risk-benefit profile.

Several other studies provide additional context and evidence regarding the use of NOACs versus VKAs in patients with valve replacement. The RE-ALIGN trial, which investigated the use of dabigatran in patients with mechanical heart valves, was terminated early due to a higher incidence of thromboembolic and bleeding events in patients taking dabigatran compared to those on warfarin.[5] The trial underscores the risks associated with using NOACs in patients with mechanical heart valves and reinforces the current guidelines that contraindicate NOACs in this population.

By contrast, the RIVER trial compared rivaroxaban to warfarin in patients with atrial fibrillation and a bioprosthetic mitral valve. The study found rivaroxaban to be non-inferior to warfarin in preventing thromboembolic events and to have a similar safety profile, supporting the potential use of NOACs in patients with bioprosthetic valves.[6] Similarly, the ENGAGE AF-TIMI 48 substudy examined edoxaban in patients with a bioprosthetic valve or valve repair and suggested that edoxaban might be a viable alternative to warfarin in this patient population, showing comparable efficacy and safety.[7] In addition, the ARISTOTLE trial provided important insights into the use of apixaban versus warfarin in patients with bioprosthetic valves, demonstrating similar efficacy and safety in preventing thromboembolic events.[8] However, none of these studies were specifically designed to address the early postoperative period.

The ESC guidelines,[1] which recommend the continued use of VKAs in mechanical valve patients and cautious use of NOACs in bioprosthetic valve patients, emphasize the need for careful patient selection and monitoring. The guidelines reflect current understanding and evidence, underscoring the need for further research to refine anticoagulation strategies in these populations.

Costa et al.'s study[4] provides preliminary evidence that NOACs may be associated with fewer adverse events compared to VKAs in the early postoperative period following MVR or mitral BVR. However, its retrospective design, single-center data, and short follow-up necessitate cautious interpretation. The ESC guidelines[1] highlight the ongoing uncertainty and the need for rigorous, prospective, randomized controlled trials to validate such findings and inform clinical guidelines.

In conclusion, while the study suggests potential benefits of NOACs, cardiologists must carefully weigh its findings against its limitations and consider patient-specific factors when choosing an anticoagulation strategy. Further research is essential to confirm the long-term safety and efficacy of NOACs in this setting, in order to ensure that clinical decisions are based on robust and comprehensive evidence.

Conflicts of interest

The author has no conflicts of interest to declare.

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