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COMMENTARY

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Novel oral anticoagulants versus vitamin K antagonists in transcatheter aortic valve replacement treated patients—Patients' vulnerability still matters

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Patients with aortic stenosis (AS) and undergoing transcatheter aortic valve replacement (TAVR) are affected by atrial fibrillation (AF) in 16%–59% of cases at different periprocedural stages, thus requiring oral anticoagulation.[1] Current 2020 ESC/EACTS Guidelines for the diagnosis and management of AF, recommend novel oral anticoagulants (NOACs) over vitamin K antagonists (VKAs) in NOAC-eligible patients (class I, LoE A). It should be noted that most AF NOAC trials demonstrating the superiority of NOACs over VKAs, enrolled only small numbers of AS patients, limiting the generalizability of these results in that particular setting. Accordingly, the current ESC/EACTS Guidelines for the management of valvular heart disease published later in 2021 do not specify the type of oral anticoagulant (OAC) but just the use of it lifelong for TAVR patients who have other indications for OAC (class I, LoE B). Thus, the question whether or not the NAOC has to be preferred still lingers.

In this issue of *Catheterization and Cardiovascular Interventions*, Memon M. M. et al. performed a systematic review and meta-analysis, not patient level, to assess the risks and benefits of these drug classes in TAVR patients affected by AF. A total of 12 studies were included (three randomized controlloed trials (RCTs) and nine observational), evaluating 12,203 patients of which 5544 had NOAC and 6660 had VKA (mean age range 71.2–84.4 years, average 81.2 years). The authors found no significant difference between NOACs and VKAs in terms of stroke or systemic embolism, major bleeding, intracranial hemorrhage, all-cause mortality, and myocardial infarction at a mean length of follow-up of 15.1 months, without any significant difference also in the subgroup analysis by study design (RCT or observational). Meta-regression analysis found heterogeneity in all-cause mortality to be significantly explained by percentage of males, mean age, and CHA_2DS_2-VASc score. The authors conclude that, according to their analysis, outcomes with NOACs do not significantly differ compared to VKAs following TAVR in patients with AF.

These results confirm those of other recently published meta-analysis on the same field,[2,3] which include the newly available ATLANTIS trial (presented at the American College of Cardiology Congress 2021) and ENVISAGE-TAVI AF trial,[4] and focus on patients with an indication for OAC. There are several limitations acknowledged by the authors, among them the absence of a patient-level data, heterogeneity of the populations, and definition of the outcomes (i.e., the definition of major bleeding was accepted as reported by individual studies and the rate of gastrointestinal bleeding is unknown). However, subgroup analysis confirmed that both RCTs and observational studies were congruent for all outcomes.

Granted that, it is noteworthy the absence of the benefit in terms of safety of the NOACs compared to VKAs. One possible explanation might be that these patients are *high-bleeding-risk* patients. This is also shown by a 24% increase in the rate of bleeding events with respect to nonvalvular heart disease patients included in the same trials.[5] This means that in these vulnerable bleeding patients the selective safer profile of NOACs on cerebrovascular events and major bleeding is not enough. In this regard, we know that the gastrointestinal bleeding is not reduced by NOAC—and might be fatal as well. Moreover, it is well known that AS is associated with acquired von Willebrand's disease and arteriovenous malformations,

increasing the risk of gastrointestinal bleeding. In addition, the frequent presence of concomitant coronary artery disease makes the scenario and the interpretations of the results even more complex, since NOAC safety depends also on the concomitant use of antiplatelet therapy (APT) and dosing.

To date, the enthusiasm for NOACs in this particular population is struggling to take off and the most appropriate OAC is still unclear. Until further scientific evidence is available, the choice of the proper OAC regime in TAVR patients affected by AF should be tailored according to clinical judgment. In patients already on OAC without bleeding, there is no indication for changing the type of OAC. In case of new introduction, the choice of the type of OAC is also based on the type of comorbidities and/or previous bleeding with APT or need to use also single or dual APT. NOAC may be an alternative to VKA in TAVI patients with AF, who are typically elderly and exhibit multiple comorbidities, especially when meeting dose reduction criteria or without concomitant APT. Definitely more science is needed, though.

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CONFLICTS OF INTEREST

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