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EDITORIAL

The challenge of interpreting comparative TAVI studies

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Over the last 20 years, the evolution in transcatheter aortic valve implantation (TAVI) has resulted in several devices becoming commercially available for selection. Transcatheter aortic valves (TAVs) exhibit significant heterogeneity in the design of their stent frame, leaflets and/or method of implantation, rendering specific TAVs potentially more or less favourable for specific patient anatomies. The anatomy of patients with severe aortic stenosis (AS) can vary significantly based on the underlying aortic valve phenotype (tricuspid, bicuspid), distribution and degree of leaflet calcification, size of the aortic annulus and aortic root, and height of the coronary ostia. Consequently, studies evaluating which valve designs perform favourably in specific anatomical scenarios are necessary to enable physicians to adopt a more patient-tailored approach, which is increasingly relevant given the expansion of TAVI into younger and more complex patient cohorts.

In this issue of EuroIntervention, Yamamoto et al[1] present a study comparing outcomes obtained with the Navitor (n=518; Abbott) versus Evolut FX (n=401; Medtronic) TAV in patients with a small aortic annulus (area <430 mm^2). Both are self-expanding TAVs, with the Navitor having an intra-annular leaflet position versus the Evolut FX having a supra-annular leaflet position. In the overall cohort (n=919), no significant differences in mean pressure gradient (mPG), effective orifice area (EOA), Valve Academic Research Consortium-3 defined procedural success or in-hospital mortality were observed between the two groups (p>0.05 for all). Following propensity score matching (n=219 patients/group), the authors report a statistically significant difference in mPG (Navitor: 8.7±5.0 mmHg vs Evolut FX: 7.8±4.4 mmHg; p=0.049), with no significant differences in severe prosthesis-patient mismatch (PPM; 1.9% vs 0.9%; p=0.405), ≥mild paravalvular leak (PVL; 34.1% vs 42.2%; p=0.084) or permanent pacemaker implantation (PPI; 15.2% vs 9.5%; p=0.075).

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The authors should be commended for this analysis derived from the well-known retrospective OCEAN-TAVI registry[2]. This study cohort, based on a Japanese population, allowed the authors to obtain a large sample size of patients with an aortic annulus size <430 mm^2. The data presented are contemporary given that only latest-generation TAVs were included, and the investigators appropriately excluded patients with a prior surgical aortic bioprosthesis, patients on haemodialysis, and patients in whom a second valve implantation was required.

Limitations such as the lack of a dedicated core lab for echocardiographic analysis, the inability to apply the results to a wider population globally, and the inherent limitations of a propensity-matching analysis are acknowledged by the authors. However, there are several other factors (and weaknesses) which need further discussion.

Firstly, we recommend caution when (over)interpreting the echocardiographic outcomes in this study. The reported 0.9 mmHg difference (Δ) in mPG between the two groups, although statistically significant, is likely to have little clinical significance. Moreover, caution is advised when comparing valve performance based solely on echo-reported pressure gradients, which itself is derived from measured flow velocities, or even worse, calculated EOAs and PPM rates. The Doppler Velocity Index should be considered a more appropriate parameter to compare aortic bioprostheses given that it is independent of the flow state (unlike gradient), left ventricular outflow tract diameter

(unlike EOA) and patient size (unlike PPM)[3]. Finally, the clinical and prognostic significance of post-TAVI echo gradients is debated given that differences in flow dynamics and pressure recovery in the aortic root can vary depending on the stent frame height and leaflet position of different TAVs[4].

Secondly, this study reports that the distribution of PVL grades and rates of ≥mild PVL significantly differed in the overall cohort (Navitor: 36.3% vs Evolut FX: 44.2%; p=0.02). The incidence of ≥mild PVL also tended to be lower in Navitor than in Evolut FX in the propensity-matched cohort (34.1% vs 42.2%; p=0.084). However, these results should be interpreted with a lot of caution. The anatomical phenotype was not considered and in heavily calcified anatomies, where the risk of PVL is increased, the Evolut FX was the preferred valve choice, as acknowledged by the authors.

Thirdly, although the authors report that the difference in PPI between the Navitor (15.2%) and Evolut FX (9.5%) cohorts did not reach statistical difference, an absolute difference of 4-5% (and a relative risk ratio of 1.5) may still be clinically relevant.

Fourth, a major limitation of this study is that the presented results only represent periprocedural outcomes. Lessons must be learnt from previous studies such as the ACURATE IDE trial (ClinicalTrials.gov: NCT03735667), in which important clinical events occurred beyond 30 days, or registry studies reporting on different types of surgical aortic bioprostheses, which despite initial promising results, later demonstrated poor long-term durability outcomes for some of the valve types.

To conclude, this substudy from the OCEAN-TAVI registry demonstrates that both the intra-annular Navitor and supra-annular Evolut FX TAVs are equivalent with regard to short-term valve haemodynamics and clinical outcomes in patients with a small aortic annulus. This highlights and emphasises once more that valve performance should not be attributed to a class effect comparing intra-annular to supra-annular TAVs or self-expanding to balloon-expandable TAVs. Instead, given the heterogeneity in TAVs, a more nuanced comparison of stent frame geometry and leaflet design, kinematics and coaptation is required in order to select the optimal TAV for a specific anatomy.

In conclusion, caution is advised when interpreting the results of comparative analyses of TAVs based on retrospective registries. Despite rigorous statistical matching algorithms, patient selection bias can never fully be avoided, especially as a patient-tailored approach to TAVI is increasingly being utilised for device selection.

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Conflict of interest statement

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