Transcatheter aortic valve replacement (TAVR) has emerged as an important treatment option for patients with severe aortic stenosis who are either inoperable or at high risk for surgical aortic valve replacement. Currently, 2 valves are approved by the Food and Drug Administration for inoperable patients, whereas 9 valves have received the CE (Conformité Européenne) mark in Europe for TAVR.

Several new-generation transcatheter valves promise to be equally effective and as safe as the first-generation valves but superior in regard to post-TAVR AR. However, none of these valves have been tested in a prospective controlled randomized clinical trial against the commercially available valves. Considering the fact that most of the new valves have fundamental design differences compared with the currently available valves in the United States and that the patient population undergoing TAVR is constantly changing, safety and effectiveness of these valves will be difficult to critique without properly controlled studies.

A number of studies for the new transcatheter valves are in the planning stages, but it appears that regulatory requirements are not necessarily mandating randomized clinical trials. It is obviously cheaper and easier to perform a study using objective performance goals as end points instead of a head-to-head randomized clinical trial. However, scientific confidence in such data may become problematic in TAVR studies. The advantages and disadvantages of the devices based on their design and working mechanism, changing characteristics of the study populations, and relatively limited number of controlled studies to be used as the basis for the objective performance goals are some of the challenges. Another option can be to use the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry, which can provide control groups from the ongoing practice of commercially available TAVR procedures. This will be an attractive option for an expedited approval pathway that will shorten the wait time for new devices in the United States. To accomplish this in a scientifically rigorous manner, the registry data will need close monitoring for quality and completeness, along with some core laboratory oversight.

Moderate AR has been associated conclusively with increased 1- to 3-year mortality, whereas the impact of mild AR on mortality remains controversial. In the randomized PARTNER (Placement of Aortic Transcatheter Valve) trial with independent core laboratory assessment of AR, mild AR was found to be associated with increased mortality. In the current study by Van Belle et al, mild AR appears to be benign, at least during the first year follow-up period. In our meta-analysis, mild AR was associated with increased mortality, but there was significant heterogeneity. An important reason underlying the inconsistency is the difficulty in accurate quantification of PV-AR by echocardiography. This difficulty is multiplied when echocardiographic images are obtained and assessed by different investigators with no centralized oversight. In the study by Van Belle et al, database quality control was performed by checking data against source documents for 10% of patients in randomly selected centers. The acquisition, assessment, and reporting of TTE, including quantification of PAR...
AR, were performed by individual centers with no centralized adjudication or core laboratory verification.4

There are echocardiographic guidelines for measurement of PV-AR using TTE and transesophageal echocardiogram.9,10

The premise is to measure the “gap” between the native valve and bioprosthesis to judge the severity. Because the gap is a 3-dimensional space that is cone shaped, the gap is a variable dependent on the height of the cross-sectional plane (Figure). Furthermore, the space is difficult to visualize in many patients because of shadowing of the valve cuffs, as well as the availability of acoustic windows, especially for TTE. Although the measurement criteria are standardized, there is a considerable intraobserver and interobserver variability. Therefore, precise classification of PV-AR into mild or moderate can be difficult. This issue is remedied to a great extent when an independent core laboratory is trusted with the analysis. Blinded review or core laboratory verification.8

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Access and Post-TAVR AR

In the current study, investigators reported post-TAVR AR to be more frequent in transfemoral (TF) TAVR compared with non-TF TAVR (17.7% versus 9.7%). This difference was present regardless of the type of the valve used. There are several potential explanations. One possible reason can be the variation of the valve placement. It is possible that the control of deployment is better if vascular access is closer to the aortic valve. It is possible that non-transcatheater aortic access allows for better coaxial deployment of the valve and less PV-AR, although this is conjectural at this time. The second possibility is that the non-TF access is not restrictive for the size of the implant and therefore there is less chance to err on the small-sized valve. This bias may result in lower “cover index” and more AR, although it was not studied in the current study. The implication is that a smaller valve is inserted via the TF route that may not seal as well.

Vulnerable Patients

The French Registry analysis provides valuable insight into patients that are most likely to be adversely affected by the post-TAVR AR. Acute change in the severity of AR was the most important determinant for ongoing mortality risk. This study highlights the fact that, if there is some degree of AR before the TAVR, post-procedure AR is better tolerated, presumably because of the chronic adjustment already made by the left ventricle.

Another vulnerable group of patients in the French Registry that was affected by the post-TAVR AR were the non-TF patients. It is possible that these patients whose comorbidity profile is worse are challenged by the stresses of the procedure although the surgical trauma is limited. Whether there is any consequence of apical suturing and possible alteration of diastolic dysfunction is a mechanism for not being able to tolerate AR remains to be studied. There are other subgroups that would be important to study for the impact of AR after TAVR, including patients with low-flow, low-gradient AS, patients with impaired ejection fraction, and patients with mitral regurgitation.

There are several limitations of this dataset that may be offset partially by the larger sample size. The TTE assessment, no core laboratory oversight, and lack of post-discharge follow-up are the main limitations. Limited information on the 3-dimensional annular size is another important limitation. Currently, most of the TAVR sizing is accomplished by
computed tomography or 3-dimensional transesophageal echocardiogram data, and cover index is typically calculated using this average diameter and not a single measurement on TTE as in the current study. We do not have readmission rates, functional status assessment, quality of life data, and repeat echocardiographic assessments to understand the consequences of post-TAVR AR beyond mortality. The predictors of AR are not completely analyzable because annular size assessed by cross-sectional measurements and details of deployment are not available. Whether contemporary 3-dimensional sizing and more accurate placement could have rendered different results for the same valves remain uncertain. Conversely, this is a real-world experience, which is arguably the strength of these data.

There are several take-home messages and some future responsibilities for the academic community highlighted by this study. The PV-AR is clinically important and is most impactful on patients without previous AR and with multiple comorbidities. Second, the registry data are a powerful component of our collective information base as long as we maintain the highest quality of the data that are collected. However, we still need the appropriately controlled studies to understand the comparative effectiveness of the new-generation transcatheter valves; the ideal would be randomized, controlled trials.

Disclosures

None.

References


Key Words: Editorials ■ aortic valve insufficiency ■ aortic valve stenosis
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