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EDITORIAL COMMENT

# Transcatheter Mitral Valve-in-Valve Replacement

## The New Gold Standard for Treating Mitral Bioprosthesis Failure?*

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The occurrence of structural valve degeneration (SVD) requiring reintervention is one of the main limitations of bioprosthetic valves, with an increased risk for clinically relevant SVD at long-term follow-up associated with bioprosthetic valves in the mitral (vs. aortic) position (1). Redo surgical mitral valve replacement (SMVR) is the current gold standard for treating mitral bioprosthetic SVD, but this operation has been associated with substantial morbidity and mortality, particularly among elderly patients (2).

SEE PAGE 1131

Transcatheter valve-in-valve replacement has emerged as a valid alternative to redo surgery for patients with surgical bioprosthesis dysfunction (3). This strategy was initially used for treating bioprosthetic aortic valve failure, and Cheung et al. (4) were the first to report, in 2009, the use of a transcatheter valve for treating mitral bioprosthesis dysfunction. However, data on transcatheter mitral valve-in-valve replacement (TMVR) remain scarce (3,5). In this issue of *JACC: Cardiovascular Interventions*, Kamioka et al. (6) report a comparison of the results of TMVR in 62 patients with those obtained with SMVR in 59 patients at 3 centers. Patients undergoing TMVR were older (mean age 75 vs. 64 years) and exhibited a higher risk profile (mean Society of Thoracic Surgeons Predicted Risk of Mortality score 12.7% vs. 8.7%). A balloon-expandable valve (Edwards SAPIEN/XT/3, Edwards Lifesciences, Irvine, California) was used in all TMVR cases, and most procedures (77%) were performed through a transfemoral-transseptal approach. TMVR was associated with a much lower rate of major bleeding and atrial arrhythmias and a shorter hospital stay. In the TMVR group, the rates of stroke, surgical conversion, and left ventricular outflow tract obstruction were 0%, 1.6%, and 3.2%, respectively. Thirty-day mortality rates were similar in the 2 groups (TMVR, 3.2%; SMVR, 3.4%), and there were no differences in residual mean transvalvular gradient (TMVR, 7.1 mm Hg; SMVR, 6.5 mm Hg) and moderate or severe mitral regurgitation (TMVR, 3.8%; SMVR, 5.6%) at 30 days between groups. At 1-year follow-up, mortality rates were similar in the TMVR (11.3%) and SMVR (11.9%) groups, and the mean transvalvular gradient was slightly higher in the TMVR group (7.2 mm Hg) compared with the SMVR group (5.5 mm Hg). Two patients (1 case in each group) required reintervention due to significant paravalvular leak.

This study represents 1 of the largest TMVR series to date and the very first attempt to compare this therapy with the gold standard, SMVR. The main limitations are related to the relatively small sample size and retrospective nature of the study, with different time periods for the 2 groups (a much more recent period for the TMVR group), a lack of adjustment for multiple confounding factors, and potential selection bias. It is also unfortunate that echocardiographic data were available in only a minority of SMVR patients (even at hospital discharge). Also notable is the significant attrition of echocardiographic TMVR data at follow-up, with only one-third

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of TMVR patients having echocardiographic data at 1 year. These shortcomings significantly diminish the investigators' ability to make meaningful comparisons between surgical and transcatheter late valve hemodynamic performance. Despite these limitations, the Kamioka et al. (6) work provides novel and very valuable data that may indeed contribute to the ongoing change in the strategy for treating mitral bioprosthesis dysfunction. Several points should be highlighted.

## PROCEDURAL AND 30-DAY RESULTS

It is remarkable that the mortality rates associated with SMVR and TMVR were much lower (<4%) than those expected on the basis of the surgical risk scores (>8% and >12% for SMVR and TMVR, respectively). Overall, the periprocedural results appeared to favor TMVR, with lower morbidity, hospitalization length, and similar mortality compared with SMVR despite the older age and higher risk profile of TMVR candidates. These results are similar to those recently reported in a recent large TMVR registry (5). It would have been interesting to have outcome data based on the type of approach used for TMVR (transseptal vs. transapical). Although the transapical approach may facilitate transcatheter valve coaxiality and positioning, one would expect overall improved outcomes with the transseptal approach by avoiding both the thoracotomy and myocardial injury.

## VALVE PERFORMANCE

The occurrence of high residual gradients has been one of the main drawbacks of transcatheter aortic valve-in-valve procedures (3). However, this has been related mainly to the treatment of small (<23-mm) surgical valves, which frequently exhibit high transvalvular gradients and moderate-to-severe prosthesis-patient mismatch immediately after the initial surgical intervention. The use of larger surgical bioprostheses in the mitral position may partially limit this issue, and this was supported by the lack of significant differences in the early valve hemodynamic parameters between SMVR and TMVR. The slightly higher transvalvular gradients at 1 year in the TMVR group should be interpreted with caution because of the very small number of patients with echocardiographic data at follow-up. In addition, paired echocardiographic data and other appropriate imaging techniques are needed to evaluate the issue of subclinical valve thrombosis following TMVR. However, the fact that most TMVR recipients receive anticoagulation would make this problem more unlikely compared with the aortic position.

Previous studies among TAVR patients have shown more effective valve sealing, preventing residual regurgitation following valve-in-valve procedures (compared with TAVR for native aortic stenosis) (3), and this was also observed in this study following TMVR, with rates of significant residual leaks (<5% at 30 days and 1 year) similar to SMVR.

## REMAINING ISSUES

**CONCOMITANT TRICUSPID REGURGITATION.** The presence of significant tricuspid regurgitation (TR) is common in patients with left-sided valve disease and is associated with poorer outcomes (7). Thus, addressing TR at the time of mitral surgery is currently recommended in many subsets of patients. Significant TR occurred in more than one-half of the patients in the study by Kamioka et al. (6), but only a small proportion of patients had tricuspid valve surgery at the time of SMVR. As expected, none of the patients in the TMVR group underwent TR repair at the time of the intervention and 70% of patients had moderate or worse TR at 1 year. Considering the negative influence of TR on clinical outcomes, this factor should probably be considered in the clinical decision-making process of those patients eligible for both TMVR and SMVR. Multiple transcatheter therapies have recently emerged for treating TR (7), with promising preliminary data on safety and efficacy for most devices. The consolidation of these techniques may represent a paradigm shift on the treatment of patients with left-sided valve disease and significant functional TR.

**MITRAL ANNULOPLASTY RINGS.** Studies evaluating TMVR for the treatment of mitral regurgitation in the presence of mitral annuloplasty rings have shown a much higher rate of residual leaks and unsuccessful procedures (3,5). It would therefore be important not to extrapolate the results of the present study (which did not include patients with mitral prosthetic rings) to the treatment of severe MR in the presence of a mitral ring, especially in the presence of encouraging results of surgical mitral re-repair for degenerative disease (8).

**VALVE DURABILITY.** The paucity of data on long-term valve durability is currently one of the major limitations of transcatheter valve therapies. This is of particular importance in the field of TMVR, in which only data at 1-year follow-up are available. Similarly, the limited amount of echocardiographic follow-up at 1 year severely weakens the findings of Kamioka et al.

(6) in that late TMVR prosthesis durability and hemodynamic performance are largely unknown and will need to be elucidated before TMVR can be widely adopted, especially among younger and low-risk surgical candidates with failed mitral bioprostheses. Although the results of Kamioka et al. (6) showing no valve failures up to 1 year following TMVR are encouraging, the precedent of an increased risk for SVD among surgical bioprostheses in the mitral position should stimulate close and continued follow-up of TMVR recipients.

## CONCLUSIONS

The treatment of failing surgical mitral bioprostheses remains a challenge. In recent years, a natural shift toward the use of TMVR has been adopted at many centers worldwide, and this was also reflected by the work of Kamioka et al. (6), with most patients undergoing TMVR instead of SMVR in the past few years. The relatively low rates of periprocedural morbidity and mortality and favorable echocardiographic parameters of valve performance in that study would support the use of TMVR as the preferred therapy in many patients with bioprosthetic mitral valve failure. A randomized trial in this field is highly unlikely in the near future, and this underscores the importance of obtaining good observational data in a larger number of patients with longer term follow-up. Pending some important issues, such as the management of concomitant functional TR and valve durability, the confirmation of these findings would establish TMVR as the new gold standard for the management of surgical mitral bioprosthesis dysfunction.

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