Prosthesis–Patient Mismatch in the Transcatheter Aortic Valve Replacement Era

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In an insightful report in 1978, Rahimtoola (1) pointed to the fact that “mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve.” He recognized that most patients have some residual aortic stenosis after aortic valve replacement and suggested that moderate or severe residual aortic stenosis may have clinical significance, although more work is needed to be done to better understand this phenomenon and identify its clinical implications.

How to Define PPM?

Definitions revolve around some measure of valve size in relation to patient size. Body surface area has been consistently used to index valve size. One argument is to use the in vitro measurements of geometric orifice area (GOA) reported by manufacturers for each size and type of prosthesis (2,3). This is a more consistent value, although whether or not it represents in vivo conditions accurately is debatable. In the recently published American Society of Echocardiography guidelines for evaluation of the prosthetic valves, the use of effective orifice area (EOA) was recommended (4). EOA is calculated in a way similar to native aortic valve area using the continuity equation and left ventricular (LV) outflow diameter, assuming a circular shape of LV outflow. These guidelines classified PPM as hemodynamically insignificant for indexed EOA >0.85 cm²/m², moderate for 0.65 to 0.85 cm²/m², and severe for <0.65 cm²/m². These cutoff values are arbitrary, which is evidenced by the use of several different values by various investigators (5). Irrespective of the cutoff value, the accurate measurement of EOA is critical in diagnosing PPM. Accordingly, common pitfalls in measurement, such as contamination with the mitral regurgitation signal and erroneous correction for malalignment of the Doppler beam, should be avoided. High flow states and the pressure recovery phenomenon are other potential sources of EOA overestimation that should be kept in mind (6).

Clinical Impact of PPM

The prevalence of mild to moderate and severe PPM range between 20% and 70% and between 2% and 11%, respectively. Wide variability is due to the differing definitions of PPM. The impact of PPM on clinical outcomes has been studied in several retrospective studies, also using variable definitions. The inconsistency of results was apparent in studies investigating the clinical impact of PPM as well. Several studies have reported increased short- (7–9) and long-term (7) mortality, deterioration in hemodynamic variables (9,10), reduced exercise tolerance (11), higher severity of PPM, confounding effects of age, sex, and other comorbidities, possible treatment biases at different centers, and the retrospective nature of all studies, most of which had relatively small sample sizes.

PPM might be an important determinant of persistent diastolic dysfunction with incomplete regression of LV hypertrophy (18). In contrast, comorbid conditions such as hypertension, older age, and coronary artery disease are associated with decreased systemic vascular resistance and increased global afterload, which may diminish the possible benefits of intervention. Assessment of valvuloarterial impedance along with LV global longitudinal strain and strain

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rate analysis may help clinicians better understand the hemodynamic impact of PPM and predict the outcomes of TAVR and LV reverse remodeling. Because LV ejection fraction is not a sensitive marker to detect the early recovery of LV systolic function after TAVR, LV global strain might be used as a more reliable method to understand changes in LV unloading pattern.

PPM in the TAVR Era

Transcatheter valves are deployed in diseased aortic valves without removal of the native valve. Furthermore, the placement of these valves is at variable height in relation to the annulus, because of deployment variability. Limited prosthesis sizes are available, requiring use of the same-size device for a relatively wide range of annular sizes (e.g., the 23-mm Edwards SAPIEN valve [Edwards Lifesciences, Irvine, California] for 17- to 21-mm annuli and the 26-mm valve for 22- to 25-mm annuli). These factors make the assessment and prevention of PPM even more challenging. In this issue of the Journal, Ewe et al. (19) present a retrospective study of patients undergoing TAVR with balloon-expandable Edwards SAPIEN valves. PPM was defined to be present when EOA was <0.85 cm²/m² and was present in 18% of the investigators’ population. They found that LV mass reduction, left atrial size reduction, and normalization of filling pressure were less pronounced in patients with PPM compared with those without. This translated to diminished reductions in symptoms, as evidenced by larger proportions of patients with no changes in New York Heart Association functional class among those with PPM.

This study is one of several focusing on PPM in patients undergoing TAVR (20–22). In these studies, moderate PPM (0.60 to 0.85 cm²/m²) was encountered in about 20% and severe PPM (<0.60 cm²/m²) in about 10% of patients undergoing TAVR. In the present study, Ewe et al. (19) were not able to characterize the impact of severe or moderate PPM on outcomes, because of a relatively small sample size. For the same reason, the impact of PPM was assessed only in a univariate analysis. Important procedural variables other than PPM could have accounted for differences in outcomes, but it is difficult to decipher from this report. It appears that most of these patients had Edwards balloon-expandable valves, but it is not clear how many of these patients had SAPIEN XT valves. Although not statistically significant, the use of smaller valve sizes and the transfemoral approach were more frequently seen in patients with PPM. Echocardiographic follow-up was carried out at 6 months. It is not clear if the differences in LV dimensions and hemodynamic parameters would decrease or increase with longer follow-up. Variability in the management of hypertension after valve replacement and the use of different medications may have contributed to the differences in hemodynamic outcomes at follow-up, but these data are not available in the present report. Furthermore, measurements were made without the help of an independent core laboratory, and analysis was done retrospectively, which may be a source of bias.

The methodology of measurement of EOA in this study needs critical evaluation. The calculation of EOA using the continuity equation requires the measurement of 3 variables: the LV outflow tract diameter, the LV outflow tract, and transprosthetic flow velocities. In previous studies, 2 methods have been used to estimate the EOAs of TAVR prostheses: some investigators have used the LV outflow tract diameter measured at the base of the prosthetic valve leaflets, whereas others used the diameter measured just proximal to the prosthesis stent (20–22). In the present study, the second method was used, which appears to be more reliable and reproducible and correlates better with gradient across the implanted transcatheter aortic valve.

This study does not focus on factors that contributed to PPM. Whether the choice of valve size, patient size, annular size, pre-existing calcification of the aortic valve apparatus, or some procedural variable such as pre- or post-dilation balloon size or positioning of the valve or measured annular size contributed to the development of PPM is unclear. Consequently, it is difficult to understand how the procedure can be modified to minimize PPM.

Over the years, surgical valves have seen multiple alterations and innovations to improve EOA. Transcatheter valves are also building on the same experience not only to improve EOA but also to potentially improve durability. It is important to recognize that the currently available transcatheter valves provide better EOA compared with surgical valves, because leaflets of these valves are mounted directly on the stents, without a sewing ring (Fig. 1). Larger EOA is necessary because the annulus is not prepared by excising calcium, as is done in surgery. Balloon-expandable and self-expanding valves have very similar GOAs in currently used valves. CoreValve (Medtronic Inc., Minneapolis, Minnesota) leaflets are mounted in the supra-annular portion of the stent to allow for larger EOA. Edwards valves are mounted to the stent, without compromising any space within the lumen. How these different valve designs of transcatheter valves will affect durability is another question with no meaningful clinical data at this time.

Finally, the clinical significance of PPM remains unclear in this patient population. Patients undergoing TAVR are high-risk patients who are typically in their 80s. It remains to be seen whether PPM equivalent to moderate nonprogressive aortic stenosis leads to any adverse outcomes in this patient population. At least on short-term follow-up as reported in the present study, there was no increase in clinical adverse events. Long-term outcomes will be determined foremost by valve durability and patient comorbidities. How PPM fits in this equation is unclear. However, less than optimal improvement in symptom relief associated with PPM is a concern and should be further investigated. Optimizing the size of the aortic annulus and the availability of more valve sizes will help in the prevention of PPM.
Although bigger is better, knowing how much bigger is possible without compromising the safety of TAVR is critically important.

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REFERENCES


