EDITORIAL COMMENT

Resolving the Prosthesis-Patient Mismatch Debate

Cheol Hyun Lee, MD, PhD

Prosthesis-patient mismatch (PPM) remains a critical issue in transcatheter aortic valve replacement (TAVR), in which the effective orifice area (EOA) of the prosthetic valve is insufficient relative to the patient's body surface area (BSA) and cardiac output requirements, leading to elevated transvalvular gradients.[1] Over the years, conflicting evidence has emerged regarding the clinical significance of PPM, especially across different populations (Figure 1). Although the adverse impact of PPM on surgical aortic valve replacement is well established,[2] its effect on outcomes after TAVR remains uncertain. Although some past studies have indicated that PPM after TAVR does not significantly affect short-term outcomes,[3,4] others have highlighted an association between PPM and poorer long-term prognosis, including increased mortality and adverse clinical events.[5-7] The ongoing debate regarding the clinical impact of PPM may be attributed to the heterogeneity of the study results, which is likely driven by differences in patient characteristics, valve types, sample sizes, and follow-up durations. Of the various studies in the literature, two are particularly important. The first is the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) registry, which enrolled 62,125 patients from a Western cohort. In this study, severe PPM after TAVR was present in 12% of the patients and was associated with higher mortality and heart failure rehospitalization after 1 year.[3] The other key study, published in 2018, focused on an Asian cohort through the OCEAN-TAVI (Optimized Transcatheter Valvular Intervention) registry,

which enrolled 1,588 patients, representing the largest Asian cohort.[5] In this study, PPM occurred in <1% of patients and was not identified as an independent predictor of 1-year mortality or rehospitalization. Conflicting results from the largest Western and Asian cohorts have fueled the debate over the clinical impact of PPM. However, upon closer examination of these two studies, the most significant difference, aside from racial factors, was the number of patients enrolled. Another key difference was the incidence of severe PPM in the two cohorts. In the Western cohort, a large patient population and a high incidence of severe PPM led to differences in 1-year mortality and rehospitalization. In contrast, although the OCEAN-TAVI registry represents the largest Asian cohort, the incidence of severe PPM was only 0.7%. This relatively low incidence, combined with the small sample size and short follow-up period, limited the statistical analysis of the impact of severe PPM on clinical outcomes. The Transpacific TAVR Registry, which previously reported on racial differences,[6] primarily attributed the discrepancy in severe PPM incidence to variations in patients' BSA between Western and Asian populations. However, the study also noted that the clinical outcome patterns did not differ between Western and Asian patients with PPM. Resolving the debate on PPM will likely require a larger number of enrolled patients and longer follow-up periods, which will enable more meaningful statistical analyses and allow for clearer conclusions regarding the true clinical impact of PPM.

The 2024 update of the OCEAN-TAVI registry on the prognostic value of PPM, reported in this issue of *JACC: Asia*,[8] presents data that may have a significant impact on the ongoing debate regarding the clinical implications of PPM. The issue of the low incidence of severe PPM has been addressed, with the number of enrolled patients increasing to 7,072 and the follow-up period extended to 3 years, thus allowing for a more robust statistical analysis of severe PPM. Unlike the findings from 2018, the incidence rate of severe

From the Division of Cardiology, Department of Internal Medicine, Keimyung University Dongsan Hospital, Daegu, Korea.

FIGURE 1 Conflicting Evidence on the Clinical Significance of Prosthesis-Patient Mismatch
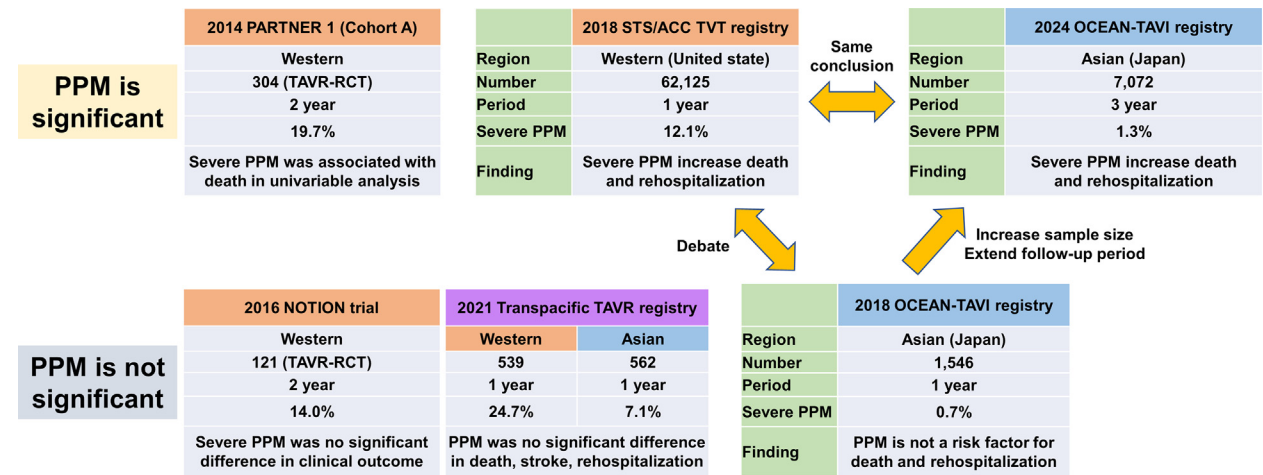
Conflicting evidence from various clinical trials and registries highlights how differences in methodologies and patient cohorts contribute to variability in the impact of prosthesis-patient mismatch on patient outcomes. NOTION = Nordic Aortic Valve Intervention; OCEAN-TAVI = Optimized Catheter Valvular Intervention – Transcatheter Aortic Valve Implantation; PARTNER = The Placement of Aortic Transcatheter Valves; PPM = prosthesis-patient mismatch; RCT = randomized controlled trial; STS/ACC TVT = Society of Thoracic Surgeons–American College of Cardiology Transcatheter Valve Therapy; TAVR = transcatheter aortic valve replacement.

PPM was reported to be 1.3%, and it was identified as an independent risk factor for 3-year mortality and rehospitalization. This result provides important insights for physicians in the context of the PPM debate. First, it reaffirms that, regardless of racial differences, severe PPM is associated with worsening clinical outcomes, mirroring the results observed in the Western cohort. Second, the study shows that the previously inconsistent results between studies were largely due to the insufficient number of patients and follow-up duration required to accurately assess the clinical significance of severe PPM. This highlights the fact that a much larger patient population than previously expected is necessary to fully understand the impact of PPM, and that previous studies may have produced conflicting results owing to these limitations. Third, the study offers important insights into moderate PPM. Both Western and Asian cohorts have shown that moderate PPM does not have clinical significance. This emphasizes the need to separate moderate and severe PPM in statistical analyses, as combining them could reduce the clarity and significance of the clinical findings.

Resolution of the PPM debate could lead to further advancements and changes in TAVR, with important implications for clinical practice. Since the introduction of TAVR, much research has focused on comparing TAVR with surgical aortic valve replacement and addressing acute device failures such as coronary obstruction or access, permanent pacemaker implantation, aortic root injury, and stroke. However, with the PPM debate potentially resolved, future research may shift toward optimizing TAVR strategies for selected patient populations. Following the recent SMART (Small Annuli Randomized to Evolut or SAPIEN) trial,[9] which examined TAVR in patients with small annuli, interest in post-TAVR hemodynamics is growing. Therefore, future research is expected to focus more on tailored TAVR device selection to achieve larger EOA, particularly in patients with large BSA, valve-in-valve procedures, or TAVR-in-TAVR scenarios. These efforts aim to improve outcomes by customizing the device choice to maximize the EOA. Furthermore, the findings from such research could drive the development of next-generation TAVR devices designed to maximize EOA. As coronary disease research has established the importance of luminal gain and improvements in coronary hemodynamics, future studies on aortic stenosis may establish specific EOA thresholds and post-TAVR hemodynamics as critical markers of clinical outcomes. These advancements will be particularly important as the TAVR candidate population becomes younger, emphasizing the need for

long-term management of patients with severe aortic stenosis. Consequently, these insights could significantly influence treatment planning for physicians, helping them select the best strategies for the lifelong management of these patients.

The updated OCEAN-TAVI registry in 2024 confirms that PPM remains a clinically relevant issue, independent of anatomical or ethnic differences. The increased cohort size and the extended follow-up have clarified that severe PPM is associated with worse outcomes, such as increased mortality and heart failure hospitalization. These findings emphasize the importance of personalized device selection and improvements in prosthesis design to reduce the occurrence of PPM. As TAVR continues to evolve and its candidate population grows younger, the long-term management of patients with severe aortic stenosis will benefit from ongoing advancements in prosthesis technology and patient-specific treatment strategies.

ADDRESS FOR CORRESPONDENCE: Dr Cheol Hyun Lee, Division of Cardiology, Department of Internal Medicine, Keimyung University Dongsan Hospital, 1035 Dalgubeol-daero, Dalseo-gu, Daegu 42601, Republic of Korea. E-mail: movicbeat@gmail.com.

REFERENCES

1. Pibarot P, Magne J, Leipsic J, et al. Imaging for predicting and assessing prosthesis-patient mismatch after aortic valve replacement. *JACC Cardiovasc Imaging*. 2019;12:149–162.

2. Head SJ, Mokhles MM, Osnabrugge RL, et al. The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27,186 patients with 133,141 patient-years. *Eur Heart J*. 2012;33: 1518–1529.

3. Herrmann HC, Daneshvar SA, Fonarow GC, et al. Prosthesis-patient mismatch in patients undergoing transcatheter aortic valve replacement: from the STS/ACC TVT Registry. *J Am Coll Cardiol*. 2018;72:2701–2711.

4. Pibarot P, Weissman NJ, Stewart WJ, et al. Incidence and sequelae of prosthesis-patient mismatch in transcatheter versus surgical valve replacement in high-risk patients with severe aortic stenosis: a PARTNER trial cohort — a analysis. *J Am Coll Cardiol*. 2014;64:1323–1334.

5. Miyasaka M, Tada N, Taguri M, et al. Incidence, predictors, and clinical impact of prosthesis-patient mismatch following transcatheter aortic valve replacement in asian patients: the OCEAN-TAVI registry. *JACC Cardiovasc Interv*. 2018;11: 771–780.

6. Park H, Ahn JM, Kang DY, et al. Racial differences in the incidence and impact of prosthesis-patient mismatch after transcatheter aortic valve replacement. *JACC Cardiovasc Interv*. 2021;14: 2670–2681.

7. Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. No clinical effect of prosthesis-patient mismatch after transcatheter versus surgical aortic valve replacement in intermediate- and low-risk patients with severe aortic valve stenosis at mid-term follow-up: an analysis from the NOTION trial. *Eur J Cardiothorac Surg*. 2016;50: 721–728.

8. Ishizu K, Kitano K, Yamamoto K, et al. Update on prosthesis-patient mismatch following transcatheter aortic valve replacement in Asian patients. *JACC Asia*. 2024;4(11):793–806.

9. Herrmann HC, Mehran R, Blackman DJ, et al. Self-expanding or balloon-expandable TAVR in patients with a small aortic annulus. *N Engl J Med*. 2024;390:1959–1971.

KEY WORDS aortic stenosis, heart failure, long-term outcomes, prosthesis-patient mismatch, transcatheter aortic valve replacement