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REPLY FROM AUTHORS: PROSTHESIS–PATIENT MISMATCH IS NOT SYNONYMOUS WITH ELEVATED TRANSVALVULAR PRESSURE GRADIENT

Reply to the Editor:

We thank Ternacle and Pibarot for their letter in which they discuss that prosthesis–patient mismatch (PPM) is not the same as an elevated gradient across a prosthetic heart valve.[1] In fact, the aim of our analysis was to validate previous results of their group published in the *Journal of the American College of Cardiology*, in which they propose the commonly used cut-off point for PPM.[2] Their study shows that an indexed effective orifice (EOAi) area of 0.85 cm^2/m^2 corresponds with the point where mean aortic gradient accelerates, which directly implies that the presence of PPM corresponds with elevated transprosthetic pressure gradients. As baseline characteristics of the analyzed cohort are missing, it also suggests that the strong and inverse curvilinear relationship between the EOAi and transvalvular gradient has no interaction with any patient characteristics, including flow status. In contrast to their results, we found a near-linear relation between EOAi and mean aortic gradient in 2171 patients with surgical stented bioprosthesis.[3] Therefore, we found the selection of any cut-off value for PPM to be an arbitrary process.

In their letter, the authors argue that in patients with normal left ventricular outflow, there remains a strong and inverse curvilinear relationship between EOAi and transprosthetic gradient. However, as normal left ventricular outflow is based on a cut-off point of indexed stroke volume (SVi), one must be aware of the overlap in measurements between SVi and EOAi. Misalignment of pulsed-wave Doppler, incorrect level of left ventricular outflow tract diameter measurement, or improper normalization with body surface area will all result in errors in the same direction. It is therefore not surprising that there is an association between SVi and EOAi, but it is unclear to what extent this is due to methodologic errors. For example, left ventricular ejection fraction, which has no overlap in measurements with EOAi, did not have an interaction with the relation between EOAi and mean gradient.[3]

If the authors are correct that flow status influences the relation between EOAi and gradient and "pseudo-severe PPM" exists, this leads to more questions than answers about the current definition of PPM. First of all, separate cut-off values according to flow tatus are required to accurately classify PPM, which emphasizes the overlap between EOAi and SVi. More importantly, it implies that EOAi is a flow-dependent parameter of hemodynamic obstruction, which questions the added value of EOAi over transprosthetic gradients. As the current definition of PPM is based on the relationship between EOAi and transprosthetic gradient, one could argue classify PPM by transprosthetic gradient. Although this classification requires separate cut-off values for normal- and low-flow patients, the independent measurement of SVi and transprosthetic gradient prevents spurious correlations based on mathematical coupling.

The authors reiterate the benefits of using projected effective orifice area (EOA) for the classification of PPM to offset the flow-dependency of measured EOA. While projected EOA is fixed for a specific valve model, it is the mean measured EOA obtained from a reference cohort. When this reference cohort consists of patients with high flow rates (ie, young active male patients) the mean, and therefore projected, EOA will be greater than a reference cohort with a lower mean flow rate (ie, small, elderly women). Although projected EOA is independent of the flow status of the patient, it is associated with the flow status of the reference cohort. As such, projected EOA can be manipulated with certain patient selection for reference studies.

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