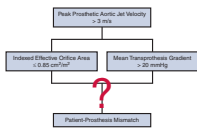


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**REPLY: RELATING THE INDEXED EFFECTIVE ORIFICE AREA AND MEAN TRANSPROSTHESIS GRADIENT TO DEFINE**



**PATIENT-PROSTHESIS MISMATCH: ARE WE SURE A RELATIONSHIP EXISTS?**

**Reply to the Editor:**

We thank Ternacle and Pibarot for their letter to the Editor and their interest in addressing patient-prosthesis mismatch (PPM) at the time of surgical aortic valve replacement (SAVR).<sup>1</sup> The senior author, Dr Pibarot, should be recognized for his seminal contributions to the study of PPM. Much of our knowledge of PPM is related to Dr Pibarot's original paper that derived indexed effective orifice area (iEOA) thresholds associated with elevated gradients to define PPM. In the study by Pibarot and Dumesnil<sup>2</sup> dating back to 2000, an exponential model was used to help determine sharp inflection points that were associated with elevated prosthetic valve mean gradients in 396 patients. Recently in the *Journal*, Vriesendorp and colleagues<sup>3</sup> re-examined this relationship using data from 5 clinical trials in which patients underwent SAVR with stented bioprostheses. Core laboratory-validated echocardiographic images from 2171 patients at 1-year postimplantation were used to assess iEOA and the transprosthetic gradient. The authors demonstrated a less-pronounced exponential relationship between iEOA and the transprosthetic gradient than was originally shown by Pibarot and Dumesnil from which the threshold of iEOA  $\leq 0.85 \text{ cm}^2/\text{m}^2$  was determined for PPM.<sup>2</sup> Vriesendorp and colleagues concluded that iEOA cutoffs currently used in guidelines were not appropriate to define PPM due to the absent exponential relationship between mean transprosthesis gradient and iEOA.

Any degree of PPM is associated with late clinical outcomes, including long-term survival and heart failure hospitalizations.<sup>4,5</sup> However, Vriesendorp and colleagues did not examine these clinically important associations with the derived thresholds for PPM. Furthermore, the context for comparison of the data is also important.

The original study from Pibarot and Dumesnil included patients with aortic homografts, pulmonary autografts, and stented and stentless bioprostheses. At the time of the original manuscript, the indications for different valve types were not known—it is probable that younger and healthier patients received homografts and autografts, whereas older patients received a bioprosthetic valve. In contrast, Vriesendorp and colleagues included only modern stented bioprostheses in the current era, where PPM is acknowledged and likely avoided by surgeons, as suggested by Fallon and colleagues<sup>5</sup> who demonstrated a decline in severe PPM from 2004 to 2014. In addition, although Vriesendorp and colleagues have derived exponential models to describe the association between iEOA and increased transprosthetic gradient, external validation is necessary to determine their generalizability.<sup>6</sup> This new fitted model by Vriesendorp and colleagues may have illustrated a different relationship in comparison with previous work due to new bioprosthetic valve types that have improved hemodynamic designs to reduce PPM. Finally, the examination of sensitivity and specificity of the models along with using receiver-operator curves to determine the cutoffs would be of interest.

Ternacle and Pibarot<sup>1</sup> have raised an important point regarding the association of transprosthetic gradient and PPM in the context of early postoperative low flow states. Ternacle and Pibarot argue that when there is a low flow across the aortic valve, which may be typical after cessation of cardiopulmonary bypass at the time of surgery, the transprosthetic gradient lacks sensitivity to identify PPM.<sup>7</sup> That said, in the article by Vriesendorp and colleagues, measurements were performed at 1-year follow-up and, as such, concerns over low flow states and subsequent low flow gradients are less of a concern.<sup>8,9</sup>

Overall, these sets of articles highlight the controversy around using iEOA as a surrogate for PPM and highlight that prevention of PPM may be the best strategy. This can be accomplished by implanting the largest valve possible with the judicious use of aortic root enlargement to avoid unacceptable postoperative transprosthesis gradients post-SAVR.<sup>10,11</sup> Future work that examines the relationship between iEOA and transprosthesis gradients to define PPM should correlate the findings to meaningful clinical outcomes, including exercise limitation and long-term mortality. We commend all authors for their ongoing work to define, predict, and prevent PPM after SAVR.

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