Enhanced freedom from prosthesis-patient mismatch with transcatheter aortic valve replacement: More to aortic regurgitation than meets the eye?

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Prosthesis-patient mismatch (PPM) is one of the less well understood “complications” of aortic valve replacement, because its manifestations are controversial and may be confounded by a wide range of baseline patient characteristics and operative variables. PPM occurs in 20% to 70% of surgical aortic valve replacement (SAVR) procedures¹ and has been associated with decreased long-term survival and freedom from heart failure, particularly in patients with left ventricular (LV) dysfunction or low-gradient aortic stenosis (AS).^{2,3} Furthermore, PPM has subclinical effects that include persistence of LV overload and impaired recovery of coronary flow reserve, which in turn may hinder the regression of LV hypertrophy and dysfunction.²⁻⁴

Regression of LV hypertrophy after aortic valve replacement is an incompletely understood phenomenon. In a recent study, researchers at the University of Ottawa Heart Institute showed that either postoperative PPM or the presence of a baseline aortic regurgitation (AR) physiology can prolong the duration and limit the completeness of LV mass regression after aortic valve replacement.⁵ Transcatheter aortic valve replacement (TAVR) is now a widely accepted intervention for patients with severe AS who are deemed to have prohibitive or high surgical risk, and it is included as such in the American and European treatment guidelines.^{6,7} Hemodynamic results with regard to the relief of AS with TAVR are excellent: for instance, studies have shown that TAVR performed on a small aortic annulus results in less PPM, likely as a result of a thinner stent frame and a tendency toward oversizing of TAVR prostheses relative to SAVR prostheses.^{8,9} Despite this favorable effect on PPM, however, long-term questions related to valve durability and persistent AR, which is found in a sizable proportion of patients who have undergone TAVR, are still incompletely answered.

In this edition of the *Journal*, Zorn and colleagues¹⁰ present their analysis of the incidence and prognosis of PPM in the TAVR and SAVR patient cohorts included in the

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Central Message

TAVR provides excellent relief from AS and freedom from PPM, but AR may have negative implications for LV mass regression.

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CoreValve US High Risk Pivotal Trial.¹¹ They showed that TAVR results in significantly lower incidence of severe PPM relative to SAVR (7.0% vs 20.7% at 1 month, and 6.2% vs 25.7% at 1 year). Despite this difference in the incidence of severe PPM, there was no difference in mortality, however, and widespread improvement in heart failure functional class was observed regardless of PPM status. Only after Zorn and colleagues¹⁰ combined the populations of patients undergoing TAVR and SAVR did they observe that there was a higher mortality in the combined severe PPM subgroups; however, it is well-known that patients with PPM are generally sicker than patients who do not have PPM, and this study was no exception.

There remain 2 important questions highlighted by this clinical and echocardiographic study and another recent, similar subanalysis of the Sapien TAVR prosthesis in the Placement of Aortic Transcatheter Valve (PARTNER A) trial.¹² First, was the impact of PPM after TAVR observed mostly in patients with LV dysfunction, as had been shown before in patients undergoing SAVR,^{2,3} and was this interaction between PPM and LV dysfunction different between the TAVR and SAVR patient groups? Second, what was the impact of residual AR (more common with TAVR) on the inhibition of LV mass regression? In the study presented in this issue, Zorn and colleagues¹⁰ focused on AR of a least a moderate degree and found no effect; however, 46% of patients undergoing TAVR (vs 12% of those undergoing SAVR) had *at least mild* AR at 1 month

after aortic valve replacement, and the effects of mild AR were not examined. Furthermore, despite a higher incidence of PPM and generally higher transprosthetic gradients, SAVR was numerically superior to TAVR with regard to absolute LV mass regression by a factor of about 2, as shown in the article's Supplemental Table 4. Thus, considering that residual AR is associated with mortality after TAVR,^{13,14} it is plausible that mild AR after TAVR is not completely innocuous and carries at least subclinical negative effects.

The evidence presented by Zorn and colleagues¹⁰ therefore, confirms that TAVR is a very good option for patients with severe aortic stenosis who would be at high risk if undergoing SAVR. One must note, however, that despite superior relief of AS with TAVR relative to SAVR in this trial population, the frequent occurrence of chronic mild AR in patients undergoing TAVR may have detrimental effects on LV mass regression. This postulated relationship warrants further study, especially as TAVR is being increasingly extended both to patients with LV dysfunction (in whom LV mass regression is particularly critical) and to patients with intermediate and low surgical risk, who would be expected to enjoy a long life and resolution of their LV hypertrophy after the relief of AS.

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