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EDITORIAL COMMENT

Prosthesis-Patient Mismatch

Another Reason for TAVR?*

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In this issue of *iJACC*, Dayan et al. (1) published a meta-analysis of prosthesis-patient mismatch (PPM) after aortic valve replacement from 58 studies involving 40,381 patients, mostly after surgical aortic valve replacement (SAVR). Their major findings were as follows: 1) moderate or greater (indexed effective orifice area [iEOA] <0.85 cm^2/m^2) PPM was associated with increased perioperative mortality; 2) severe (iEOA <0.65 cm^2/m^2) PPM was associated with increased long-term mortality, especially in patients undergoing concomitant coronary artery bypass graft (CABG); and 3) the impact of PPM on mortality was less in patients with higher body mass

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index. This carefully performed meta-analysis provides an opportunity to address the following questions: 1) Why is the iEOA used to define PPM, and how were the cutoff values chosen? 2) How does PPM cause increased mortality after aortic valve replacement? 3) Why does concomitant CABG increase perioperative mortality in patients with PPM? 4) Why is mortality not influenced by PPM in patients with large body weight? 5) Is less severe PPM partly responsible for a better clinical outcome with transcatheter aortic valve replacement (TAVR) compared with SAVR (2,3)?

INDEXED EFFECTIVE ORIFICE AREA TO DEFINE PPM

An early hemodynamic validation of echocardiography was performed in patients with aortic stenosis in the early 1980s. Aortic valve gradients and EOA derived from 2-dimensional/Doppler echocardiography were shown to correlate well with invasively obtained measurements (4). Subsequently, the accuracy of Doppler echocardiography in aortic bioprostheses was validated (5). Pressure gradient across an aortic valve varies with cardiac output, which in turn is mostly determined by body surface area (BSA), and the iEOA (EOA divided by BSA) was shown to correlate well with the mean gradient across the aortic bioprosthesis (6). These observations established iEOA as the standard means to express the area of an aortic bioprosthesis. The relationship between pressure gradient and iEOA is curvilinear and the gradients of aortic prosthesis were shown to increase exponentially when iEOA is <0.85 cm^2/m^2. Therefore, moderate PPM was defined as an iEOA <0.85 cm^2/m^2 and severe PPM as an iEOA <0.65 cm^2/m^2.

ASSOCIATION BETWEEN PPM AND MORTALITY

The development of PPM was observed more frequently in older patients, women, those with hypertension, diabetes, and a larger BSA. Many of these characteristics are similar to those present in patients with heart failure with preserved left ventricular ejection fraction. They have a smaller left ventricle and significant diastolic dysfunction. Correspondingly, in the CoreValve US Pivotal High Risk Trial (7), the patients who developed PPM after TAVR or SAVR were found to have numerically or significantly smaller baseline stroke volume, respectively, compared with the patients without PPM (69.6 ± 16.9 ml vs. 76.5 ± 23.9 ml; p = 0.21 after TAVR and 69.2 ± 18.1 ml vs. 77.5 ± 20.4 ml; p = 0.003 after SAVR). Mitral inflow deceleration time was significantly shorter (205 ± 65 ms vs. 236 ± 81 ms; p = 0.002), indicating higher filling pressure in patients with PPM after SAVR. Because these patients had a smaller heart, severe PPM was more frequent in both TAVR

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and SAVR groups when the aortic annulus diameter was <20 mm (8). One- or 2-year mortality was numerically or significantly higher in patients with severe PPM in both SAVR and TAVR groups as demonstrated by the PARTNER (Placement of Aortic Transcatheter Valves) trial (9) and the CoreValve US Pivotal Trial (7), but its impact on mortality was more significant after SAVR. Both trials showed that stroke volume and left ventricular cavity size were further significantly reduced immediately after SAVR, whereas there was no such reduction after TAVR. Moreover, the patients with severe PPM developed acute kidney injury more frequently after SAVR, but not after TAVR (7). Therefore, the combination of lower stroke volume and higher filling pressure at baseline, further reduction in stroke volume, and the development of renal injury post-operatively may explain the higher perioperative and overall mortality in patients with severe PPM after SAVR.

WHY DOES CORONARY ARTERY BYPASS SURGERY INCREASE MORTALITY WITH PPM?

Concomitant CABG increases the duration of surgery with cardioplegia, which possibly affects the myocardium. It was also shown that the rate of coronary flow reserve is reduced in patients with PPM (10). To understand the additional impact of CABG, it will be necessary to compare post-operative hemodynamics between the patients who undergo SAVR with or without CABG. The meta-analysis data, therefore, suggest that TAVR plus percutaneous coronary intervention may be preferable to SAVR and CABG in patients with severe aortic stenosis and coronary artery disease in whom PPM is anticipated.

PPM AND BODY SIZE

The fact that PPM does not have an impact on mortality in overweight patients (1,11) may be related to how BSA is calculated. There are several formulae used to calculate BSA; the most common, which is used to index the aortic EOA, is the one proposed by Dubois and Dubois in 1916 (12) as: BSA = $(W^{0.425} \times H^{0.725}) \times 0.007184$. This formula was derived from 9 infant and adult subjects with body weights ranging from 6 to 93 kg. When BSA was measured in 401 subjects by Gehan and George (13), the DuBois formula overestimated BSA by 15% in ~15% of cases. Therefore, further studies are needed to redefine the indexation of EOA in overweight patients.

PPM IN TAVR VERSUS SAVR

Both the PARTNER and CoreValve randomized trials demonstrated that PPM was less common after TAVR than after SAVR (7,8). In both trials, mortality was significantly higher in patients with severe PPM, although the mortality rate was higher in the SAVR group, and the higher mortality after SAVR was more striking for the first 3 months after the intervention (2,3,14). It is possible that less PPM after TAVR was in part responsible for the better 1- to 2-year clinical outcomes after TAVR versus SAVR (2,3). Therefore, every effort should be made to avoid or prevent PPM especially in patients with a reduced stroke volume, increased diastolic filling pressure, or coronary artery disease requiring revascularization. Also, these features and factors associated with developing PPM and worse clinical outcome after aortic valve replacement should be considered in choosing SAVR versus TAVR in patients with severe aortic stenosis.

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