Prosthesis patient mismatch in aortic valve replacement: possible but pertinent?

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Aortic valve replacement (AVR) is now the second most commonly performed cardiac operation and with an increasingly elderly population, the number of such procedures will inevitably continue to grow.\(^1\) In 1978, Rahimtoola\(^2\) defined the term prosthesis patient mismatch (PPM) to describe the situation in which the effective orifice area (EOA) of a prosthetic valve, after implantation, is smaller than that of the native valve. Although described nearly three decades ago, there are several reasons why PPM has only more recently become much more openly debated. First, PPM was initially overshadowed by the more immediate issues of operative mortality and major morbidity. Second, by definition, all prosthetic valves must therefore have at least some degree of PPM; over 90% of AVR still use prostheses with a sewing ring, or have struts, hinge mechanisms, and rigid carbon or relatively stiff bioprosthetic leaflets. Third, and most importantly, as moderate aortic stenosis can be tolerated over long periods with excellent functional status and well-preserved ventricular function, the clinical relevance of all but the most severe PPM has remained uncertain.

In the last decade, however, as Pibarot and colleagues sub-classified PPM more precisely according to the effective orifice index area (EOIA) of a prosthetic valve as mild (\(>0.85\text{cm}^2/m^2\)), moderate (\(0.65-0.85\text{cm}^2/m^2\)), or severe (\(<0.65\text{cm}^2/m^2\)),\(^3\) several studies have debated whether PPM affects short and long-term survival as well as functional status.\(^4\)–\(^11\) On the other hand, surgical procedures designed to avoid PPM, by enlarging the aortic root, increase the complexity of the operation and its operative mortality even in the best centres.\(^12\) So is there appropriately compelling evidence that the potential detrimental effects of PPM merit the performance of more complex and higher risk operations?

Four crucial considerations regarding PPM and outcome

Intuitively, PPM should impact adversely on clinical outcome, but establishing this beyond reasonable doubt is bedeviled by several facts. First, and most significantly, patients at the highest risk of PPM are those who are already at the highest risk from surgery. PPM is most common in patients with small aortic roots and this occurs most frequently in the elderly (especially females) who are also more likely to have severe coronary artery disease and poorer cardiac function and are therefore already at a higher risk from surgery. Accordingly, PPM could almost be considered as a ‘surrogate’ variable for other risk factors and as such even multivariate analysis can only partially, at best, discriminate between patient-related and prosthesis-size confounding factors.

Second, the EOIA is a functional measurement (derived echocardiographically from the continuity equation), which is dependent not only on the characteristics of the prosthesis but also on the properties of the left ventricular and aortic outflow tract. EOIA cannot therefore be established before prosthesis insertion and as there are few large cohort studies with serial measurements of EOIA, rigorously performed at rest and exercise, for different valve models and sizes, there is wide variability of published EOIA data. This seriously questions the relevance of several studies, not only composed of numerous valve types (mechanical and bioprosthetic, stented and stentless, old and new, etc.) but which have used published fixed-reference values to calculate EOIA.

A third confounding factor is the difference between EOIA and the indexed internal geometric orifice area (GOA) of the prosthesis. Although both are related to the internal diameter of the prosthesis, in contrast to the EOIA, the GOA is non-functional, \textit{ex vivo}, static measurement of the internal diameter. Whereas the EOIA has been shown to consistently correlate with post-operative gradients and haemodynamics that relationship with the GOA is less obvious. Because of the square relationship between gradient and EOA and that a decreasing EOIA correlates exponentially with the gradient, a marked increase in gradient only occurs when the EOIA falls below 0.85 cm\(^2/m^2\).\(^4\) Blackstone \textit{et al.}\(^10\) have calculated that the equivalent point for an indexed GOA is 1.2 cm\(^2/m^2\), and this may explain the less obvious relationship with pressure gradients and haemodynamics in the few studies which have used indexed GOA.

The fourth complicating factor is increasing recognition of marked discrepancies between the manufacturer labelled and actual diameter of the valve prosthesis.\(^13\)–\(^17\) Failure to...
account for this has almost certainly contributed to a frequent inability in the literature to relate labelled size of valves to haemodynamic performance.

PPM and short-term survival following AVR

The effect of PPM on short-term mortality following AVR is conflicting with four studies reporting a positive association,\textsuperscript{5,6,8,10} and two studies reporting no association.\textsuperscript{7,11} The strongest evidence that PPM increases operative mortality after AVR is by Pibarot and coworkers.\textsuperscript{5} In 1266 consecutive AVR patients, the 30-day mortality was 4.6\% in the 62\% of patients without PPM, but was doubled with moderate PPM and increased 11-fold with severe PPM. Although patients with moderate and severe PPM had significantly more risk factors including impaired left ventricular function, older age, female gender, coronary artery disease, and emergent/salvage surgery, the authors nevertheless concluded that PPM was a strong and independent predictor of short-term mortality. Likewise, Rao et al.\textsuperscript{6} also noted an increased operative mortality (8 vs. 5\%) in the 8\% of their 2891 AVR patients with PPM, but who similarly had a higher incidence of other risk factors. Finally, Blackstone et al.,\textsuperscript{10} using multivariable hazard domain analysis with balancing score and risk factor adjustment in over 13,000 AVR patients from nine centres, reported that PPM increased the operative mortality by 1–2\%. In contrast, two other studies correcting for differing baseline factors and involving 892\textsuperscript{1} and 1563\textsuperscript{2} patients, respectively, found no increase in short-term mortality with PPM.

A possible explanation for these apparently conflicting results might be an interaction of PPM with pre-existing impairment of left ventricular function. In a multivariate analysis of 52 patients undergoing AVR with a left ventricular ejection fraction below 35\%, the only predictor of surgical mortality was smaller prosthesis size.\textsuperscript{18} In an observational study of 1103 patients undergoing AVR with a stentless bioprosthesis, baseline left ventricular mass index and PPM were the strongest predictors of the extent of post-operative LV mass regression, implying a more powerful effect of PPM in the impaired ventricle.\textsuperscript{19}

PPM and cardiac failure following AVR

Four studies have addressed the relationship of PPM and non-PPM to cardiac failure after AVR. Three studies reported an association between PPM and subsequent heart failure but also noted, somewhat counter-intuitively, that this did not contribute to long-term mortality.\textsuperscript{4,6,11} In one of these reports, Ruel et al.\textsuperscript{11} reported that PPM defined as an EOIA <0.80 cm\textsuperscript{2}/m\textsuperscript{2} was an independent predictor of post-operative congestive heart failure, but not if PPM was defined as an EOIA <0.85 cm\textsuperscript{2}/m\textsuperscript{2}. In contrast to these three studies, Hanayama et al.\textsuperscript{8} found no association between PPM and heart failure in their series of 1129 patients.

PPM and long-term survival following AVR

Seven studies, including those which reported an adverse effect of PPM on short-term survival or an increased incidence of cardiac failure have also addressed the effect of PPM on long-term survival in more than 20,000 patients followed for 5–15 years.\textsuperscript{4,6–11} The consistent observation in these studies is the absence of any adverse effect of PPM on long-term survival. Individually, the most definitive study is that of Blackstone et al.,\textsuperscript{10} who followed over 13,000 AVR patients for a mean of 5 years and up to 15 years. After adjustment for other pre-operative risk factors, the authors could identify no adverse effect of PPM on long-term survival.

PPM and functional recovery after AVR

This question was recently addressed in a study from the Cleveland Clinic in 1108 patients undergoing AVR and whose functional post-operative recovery was assessed by the Duke Activity Status Index (DASI) 8 months after surgery.\textsuperscript{20} Overall, there was a significant improvement in post-operative functional recovery in all AVR patients, but no measure of valve orifice area could be correlated with functional recovery. On the other hand, female sex, increasing age, and pre-operative renal impairment were associated with a poor functional recovery.

Surgical options and risks for avoiding PPM

The potential risk of PPM has led some surgeons to recommend manoeuvres to enlarge the aortic annulus or root. Although these procedures may be technically successful in permitting implantation of a larger-sized prosthesis, they also increase the complexity of the procedure and, more importantly, the operative risk. Although some authors have reported excellent results,\textsuperscript{21} Sommers and David\textsuperscript{12} described an increase in operative mortality from 3.5 to 7.1\% in 98 of 530 patients who underwent patch enlargement or the aortic annulus to avoid the risk of PPM. Thankfully, there are now newer generation mechanical and bioprosthetic valves with significantly superior haemodynamics, which should allow avoidance of root enlargement in all but the most potentially severe cases of PPM.

Summary and conclusions

Most patients undergoing prosthetic AVR will ‘technically’ have some degree of PPM, but this is rarely severe and patients at the highest risk of significant PPM are those who are already at the highest risk from surgery. Although it is possible that severe PPM may result in a slight increase in operative mortality, and especially in the setting of pre-existing impaired ventricular function, there is general agreement that PPM, even when severe, does not adversely affect long-term survival. Use of newer generation aortic prosthesis with superior haemodynamics may avoid the need for enlargement of the aortic root/annulus where significant PPM is likely.

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References


