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Influence of Prosthesis-Patient Mismatch on Survival with Aortic Valve Replacement

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1. Introduction

Prosthesis-patient mismatch (PPM) was first described over 30 years ago (Rahimtoola, 1978) for aortic valve replacement: when the in vivo effective orifice area (EOA) of the prosthetic valve is less than that of the native, non-diseased, human valve. Extensive documentation on the role of PPM after aortic valve replacement (AVR) particularly addresses left ventricular mass regression and patient survival. Controversy continues about the influence of PPM on patient survival, both early and late mortality. Many studies (Pibarot and Dumesnil, 2000; Muneretto et al., 2004; Mohty et al., 2006; Tasca et al., 2006; Moon et al., 2006; Florath et al., 2008; Mohty et al., 2009; Blais et al., 2003) report PPM to be an independent predictor of mortality while others (Jamieson et al., 2010; Kato et al., 2007; Vicchio et al., 2008; Mascherbauer et al., 2008; Monin et al., 2007) showed no significant effect of PPM on patient outcome. There is also debate about whether the control of PPM reduces congestive heart failure and regression of the left ventricular mass, thereby contributing to improved survival. Several Canadian centers have been actively involved in this area of research, namely the Laval University group led by P. Pibarot, J.G. Dumesnil and D. Mohty, the UBC group led by W.R.E. Jamieson, and the University of Ottawa group led by M. Ruel and A. Kulik.

PPM is categorized by Pibarot and Dumesnil (2000), Mohty et al. (2009), and Jamieson et al. (2010) as normal (EOA index (EOAI) of > 0.85 cm² / m²), mild-to-moderate (> 0.65 cm² / m² to ≤ 0.85 cm² / m²), and severe (≤ 0.65 cm² / m²). Tasca et al. (2006) defined PPM as an EOAI of ≤ 0.80 cm² / m², Moon et al. (2006) as an EOAI of < 0.75 cm² / m², while Ruel et al. (2004), Kulik et al. (2006), Kato et al. (2007), and Monin et al. (2007) as EOAI of ≤ 0.85 cm² / m²; Florath et al. (2008) and Vicchio et al. (2008) chose 0.60 cm² / m² as the cutoff between moderate and severe PPM. As can be seen, there is no clear consensus on the exact definition of PPM; this lack of consensus may contribute at least in part to the observed discrepancies in the conclusions of the studies. The studies also differ in the length of their patient follow-up. Jamieson et al. (2010) report survival to 15 years, Moon et al. (2006) and Mohty et al. (2009) to 12 years, and the majority of the other publications on the topic of PPM report survival from 4 to 8 years (Mothy et al. 2006; Tasca et al., 2006; Florath et al., 2008; Kato et al., 2007; Mascherbauer et al., 2008; Monin et al., 2007). These differences may also contribute to the different conclusions reached.

It should be noted that the indication for surgical management of aortic stenosis is symptomatic severe aortic stenosis (< 1.0 cm^2 valve area). In the majority of patients, this is equivalent to an EOAI at or below the level of severe mismatch by our definition.

2. The influence of PPM on postoperative patient outcomes

The objective of our study (Jamieson et al., 2010) on 3,343 patients having AVR for severe aortic stenosis or mixed aortic stenosis/insufficiency was to determine the predictors for all levels of PPM on mortality and to determine if there is a relationship between PPM and other predictors of survival. The prostheses used were contemporary stented bioprostheses (2493) and mechanical prostheses (850). More specifically, 667 patients had Carpentier-Edwards PERIMOUNT pericardial prostheses (Edwards Lifesciences, Irvine, CA), 1250 patients had Carpentier-Edwards supra-annular porcine prostheses, 576 patients had Medtronic Mosaic porcine prostheses (Medtronic, Minneapolis, MN), 462 patients had St. Jude Medical mechanical prostheses (St. Jude Medical, St. Paul, MN), and 388 patients had CarboMedics mechanical prostheses (Sorin-CarboMedics, Saluggia, Italy) (Figure 1). There is a misconception with the Carpentier-Edwards supra-annular aortic valve for the early version (prior to 1985) of the mitral valve failed because of stent-post dehiscence due to excessive trimming of the aortic wall; however, this failure mode was identified in only one aortic prosthesis before the manufacturing trimming was changed (Jamieson et al., 2005; Jamieson et al, 2009). The level of PPM was classified for each patient based on reference EOAs and size for each prosthesis in the published literature. The patients considered for the study had their first aortic valve replacement. Patients who had a subsequent valvular replacement were censored alive on the date of the reoperative procedures. This concept was to avoid a hemodynamically different prosthesis at the time of reoperative explantation.



(Standard, HP & Regent)

Fig. 1. Contemporary prostheses used in Jamieson et al. (2010)

The results of Jamieson et al. (2010) (N = 3343) are compared with those of Molty et al. (2009) (N = 2576); J.G. Dumesnil and P. Pibarot, two of the more prominent investigators in the area of PPM, were also authors of the 2009 study.

	Jamieson et al. 2010 (Overall) UBC Study			Mohty et al. 2009 (Late) Laval Study		
	NS PPM (N = 3343)	Moderate PPM (N = 1547)	Severe PPM (N = 212)	NS PPM (N = 1739)	Moderate PPM (N = 797)	Severe PPM (N = 40)
Pre-operative da	ıta 🛛 📿				$) (\bigtriangleup)$	
Age, yrs	66 ± 11	69 ± 10	69 ± 12	68 ± 10	71 ± 9	69 ± 11
Female, %	29	36	57	33	50	67
BSA, m ²	1.8 ± 0.2	1.9 ± 0.2	2.0 ± 0.3	1.8 ± 0.2	1.8 ± 0.2	1.9 ± 0.3
BMI, kg/m ²	26 ± 4	28 ± 5	32 ± 8	26 ± 5	29 ± 5	32 ± 7
Hypertension	19	27	28	54	59	68
NYHA class III/IV	77	75	68	61	68	67
LVEF < 50%, %	19	19	18	19	17	18
Operative data						
Mechanical prosthesis, %	32	19	23	24	14	43
Prosthesis size ≤21mm, %	14	42	91	16	38	80
Concomitant CABG	40	47	44	43	46	58
EOAI, cm ² / m ²	0.99 ± 0.15	0.76 ± 0.05	0.60 ± 0.04	1.10 ± 0.20	0.80 ± 0.05	± 0.04

NS = nonsignificant; PPM = prosthesis-patient mismatch (see text for description of the categories); BSA = body surface area; BMI = body mass index; NYHA = New York Heart Association; LVEF = left ventricular ejection fraction; CABG = coronary artery bypass grafting

Table 1. Descriptive preoperative and operative data of the two patient cohort studies: Overall (2010) and Late (2009)

As can be seen, the preoperative and operative characteristics of both cohorts are quite comparable, with the exception of hypertension and female gender, both of which higher in the Mohty et al. cohort. Also, 46.3% of patients were classified as having no PPM, 47.4% as mild-to-moderate PPM, and 6.3% as severe PPM in the Jamieson et al. cohort, whereas 67.5% of the patients had no PPM, 30.9% had moderate PPM, and 1.6% had severe PPM in the Mohty et al. cohort. The Jamieson et al. data analysis was based primarily on overall survival (early + late), whereas Mohty et al. took only late mortality into account because early mortality in the same cohort had already been analyzed by Blais et al. (2003).

Jamieson et al. found no significant difference in early mortality between the EOAI categories (no PPM: 3.4%, mild-to-moderate PPM: 3.5%, and severe PPM: 2.8%), or in late mortality (no PPM: 33.0%, moderate PPM: 30.2%, and severe PPM: 29.2%). The freedom from cardiac death by EOAI categories was also not significant (no PPM: 68.7 \pm 2.4%, moderate PPM: 68.9 \pm 2.6%, and severe PPM: 58.9 \pm 9.7%, p = 0.699). In addition, the freedom from valve-related mortality was not significantly different by EOAI categories (no

PPM: 84.3 ± 2.0%, moderate PPM: 85.7% ± 1.9%, and severe PPM: 76.8 ± 9.6%, p = 0.998). The overall (early + late) survival, at 15 years, was $38.1 \pm 2.1\%$ for no PPM, $37.0 \pm 2.2\%$ for mild-moderate PPM, and $22.1 \pm 6.5\%$ for severe PPM (no PPM versus severe PPM: p=0.040) (Figure 2).

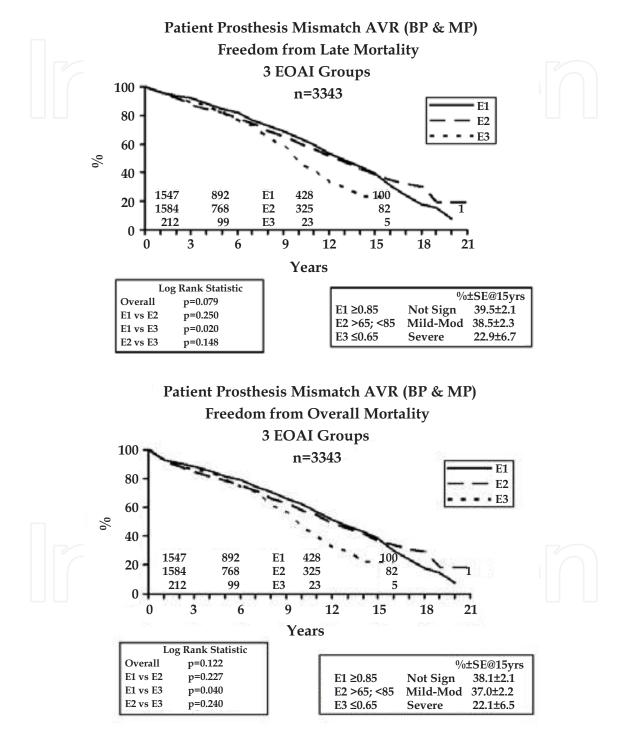


Fig. 2. Freedom from late and overall mortality by three effective orifice area index (EOAI) groups (N = 3343) (Jamieson et al., 2010). E1 (solid line), not significant; E2 (long-dash line), mild to moderate; and E3 (short-dash line), severe. (AVR = aortic valve replacement; BP = bioprosthesis; MP = mechanical prosthesis)

However, Mohty et al. found survival to be significantly lower for patients with severe PPM (5-year survival: no PPM: $84 \pm 1\%$, moderate PPM: $81 \pm 2\%$, severe PPM: $74 \pm 8\%$; 10-year survival: no PPM: $61 \pm 2\%$, moderate PPM: $57 \pm 3\%$, severe PPM: $40 \pm 10\%$). Freedom from cardiovascular-related death was also found to be significantly lower in patients with severe PPM (5-year survival: no PPM: $93 \pm 1\%$, moderate PPM: $90 \pm 1\%$, severe PPM: $78 \pm 7\%$; 10-year survival: no PPM: $81 \pm 2\%$, moderate PPM: $77 \pm 3\%$, severe PPM: $50 \pm 11\%$).

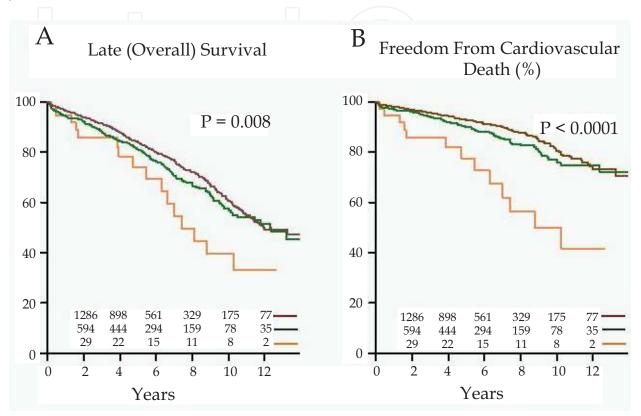


Fig. 3. Late overall survival and freedom from cardiovascular death (from Mohty et al., 2009). Brown line indicates nonsignificant prosthesis-patient mismatch (PPM); green line indicates moderate PPM; orange line shows severe PPM

The conclusion by Mohty et al. that severe PPM is an independent predictor of late mortality in patients undergoing AVR differs from the conclusion by Jamieson et al. that PPM is not a predictor of survival. It should be noted that the severe PPM group consisted of 40 patients (1.6%) in the Mohty cohort whereas it consisted of 212 patients (6.3%) in the Jamieson cohort. The very small percentage of patients with severe PPM in the Mohty et al. study could be attributed to the fact that [1] only patients who survived through the short-term period following AVR were included (whereas all patients undergoing AVR was included in the Jamieson et al. study), and [2] the short-term mortality was much higher in the Mohty cohort (7 out of 27 patients with severe PPM, 25.9%), compared with the Jamieson cohort (6 out of 212, 2.8%), and therefore not as many patients in the severe PPM survived past the early period to be included in the Mohty et al. study. The finding of severe PPM as a significant predictor of survival may be purely related to the small group size. In other words, if the group had consisted of more patients, severe PPM may not have been found to be an independent predictor. The discrepancy between the findings of these two studies warrants further investigation.

In Jamieson et al., age, NYHA class III/IV, concomitant CABG, renal failure and dialysis, and emergent preoperative status were found to be predictors of early mortality (114/3343, 3.4%) on multivariate analysis. Because a univariate analysis of the various EOAI categories showed no significance in early mortality, there was no need for a multivariate analysis on PPM versus early mortality. A study by Blais et al. (2003) revealed LVEF < 40%, infectious endocarditis, emergent status, cardiopulmonary bypass time, chronic lung disease, and moderate-severe PPM to be independent predictors of early mortality (58/1266, 4.6%). Again, the short-term mortality in the severe PPM category was much higher in Blais et al. (7 out of 27 patients with severe PPM, 25.9%) than in Jamieson et al. (6 out of 212 patients, 2.8%), which may have contributed to the significant finding by Blais et al. that severe PPM was an independent predictor of survival (Figure 4). It is not clear why early mortality was so high in Blais et al.

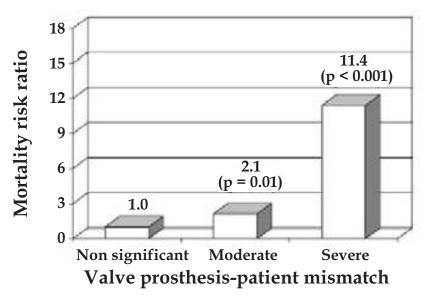


Fig. 4. Relative risk ratio for short-term mortality according to the presence and severity of valve prosthesis-patient mismatch (from Blais et al., 2003). Numbers above the bars indicate the relative risk ratio for mortality compared with the group with nonsignificant mismatch

The predictors for late mortality, identified in a multivariate analysis in Jamieson et al. were age, male gender, NYHA functional class III/IV, concomitant coronary artery bypass, LVEF < 35%, BMI < 18, BMI > 35, bioprosthesis, preoperative congestive heart failure, diabetes mellitus, renal failure, and chronic obstructive pulmonary disease. In comparison, Mohty et al. (2009) found age, coronary artery disease, diabetes, renal failure, chronic lung disease, mechanical prosthesis, and severe PPM to be multivariate predictors of late mortality.

Jamieson et al. found EOAI to have no predictive effect on survival, whether early, late, or overall, despite the survival curves differing by EOAI categories ($38.1 \pm 2.1\%$ 15-year overall survival for no PPM, $37.0 \pm 2.2\%$ for mild-to-moderate PPM, and $22.1 \pm 6.5\%$ for severe PPM). The reasons for the differences in survival curves are related to the complexity of the patients in the three categories, especially the category of severe PPM for ≤ 60 years and ejection fraction $\leq 50\%$, rather than a direct contribution from PPM.

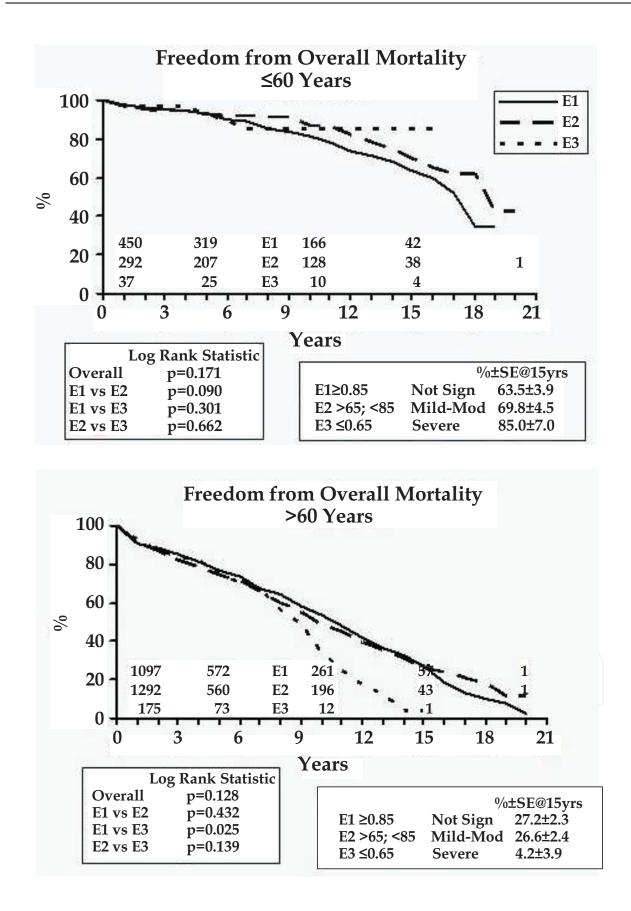
Survival was adjusted in Jamieson et al. to determine the effect of covariates (EOAI, age, BMI, and EF). Severe EOAI had no relationship on adjusted survival for the evaluated covariates, except for very low level of significance for EF > 50%.

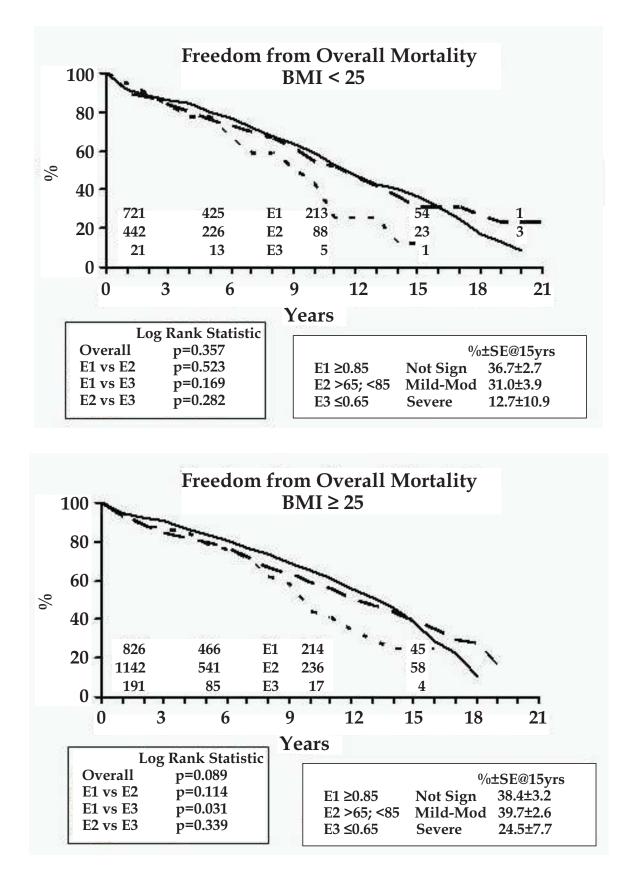
The influence of BMI was further evaluated (Yamashita et al., personal communication). Overweight or mild-to-moderately obese patients had a lower risk of early mortality, while underweight and severely obese patients had a higher risk of late mortality. When patients were analyzed as normal/underweight or overweight/obese, those with a normal EOAI had better 15-year survival than those with severe PPM. After adjusting for EOAI, age > 60 years and EF \leq 50% indicated a higher risk of overall (early + late) mortality within BMI categories. These results suggest that BMI is associated with survival after AVR and that PPM may modify the effect.

EOAI was also evaluated as a continuous variable (along with other variables except EF), as well as a categorical variable, which revealed that EOAI was not an independent risk factor for late (> 30 days) or overall mortality. The predictors, otherwise, were not different from the categorical modeling except for the elimination of valve size and the addition of BMI for early mortality. Valve type was eliminated for late mortality and overall mortality.

The survival curves in Jamieson et al. show that severe PPM (EOAI of $\leq 0.65 \text{ cm}^2/\text{m}^2$) reduces survival for patients > 60 years old but not for patients \leq 60 years old, that severe PPM reduces survival for patients with a BMI ≥ 25 kg/m² but not for those with a BMI < 25 kg/m^2 , and that severe PPM reduces survival for patients with an ejection fraction > 50% but not for those with an $EF \le 50\%$ (Figure 5). In comparison, Mohty et al. found that severe PPM was associated with increased mortality in patients < 70 years old but not in older patients, and that it significantly affected survival in patients with a BMI < 30kg/m² but not in those with a BMI \geq 30kg/m² (Figure 6A, 6B, 6C, 6D). They also found moderate-to-severe PPM to be an independent predictor of late mortality in patients with a pre-operative LVEF < 50% but not in those with preserved LV systolic function (Figure 6E, 6F). With regard to these discrepancies, it is worth noting that there were only 21 patients in the Jamieson et al. BMI < 25 kg/m² severe PPM group and 39 patients in the LVEF \leq 50% severe PPM group, while for the severe PPM subset of the Mohty cohort, there were fewer than 20 patients in each of the < 70 years old, \geq 70 years old, BMI < 30 kg/m², and BMI \geq 30kg/m² subgroups. We therefore believe that the discrepancies in the above results may be purely due to random variations in the small data sets, and that if given an adequate number of cases in each of the categories, there may be no differences in the results between the Jamieson et al. and the Mohty et al. groups.

Ruel et al. (2006) found that PPM primarily affected patients with impaired left ventricular function at the time of AVR, and patients in whom PPM was associated with decreased overall long-term survival, lower freedom from heart failure, and diminished left ventricular mass regression. Also, an EOAI $\leq 0.85 \text{ cm}^2 / \text{m}^2$ did not have a significantly detrimental effect in patients with normal preoperative left ventricular function. However, the authors pointed out that PPM might have been found to have a significant effect in the normal LV function cohort had they evaluated cases with severe mismatch ($\leq 0.65 \text{ cm}^2 / \text{m}^2$). An earlier study by Ruel et al. (2004) had shown that although PPM had significant effects on cardiac end points (occurrence of congestive heart failure, etc), it had no effect on overall survival after AVR. Kulik et al. (2006) found that patients with low-gradient aortic stenosis (LGAS, defined as an aortic valve area of < 1.2cm², a mean transvalvular pressure gradient of < 40 mmHg, and a LVEF of < 50%) have worse long-term outcomes after AVR, and that PPM further adversely affects the long-term outcomes of LGAS patients and should therefore be avoided in this population.





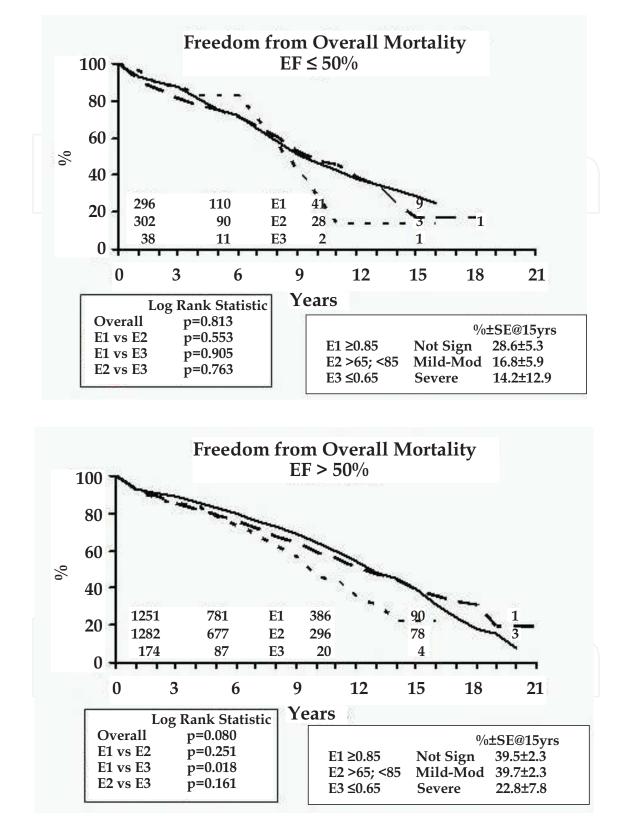
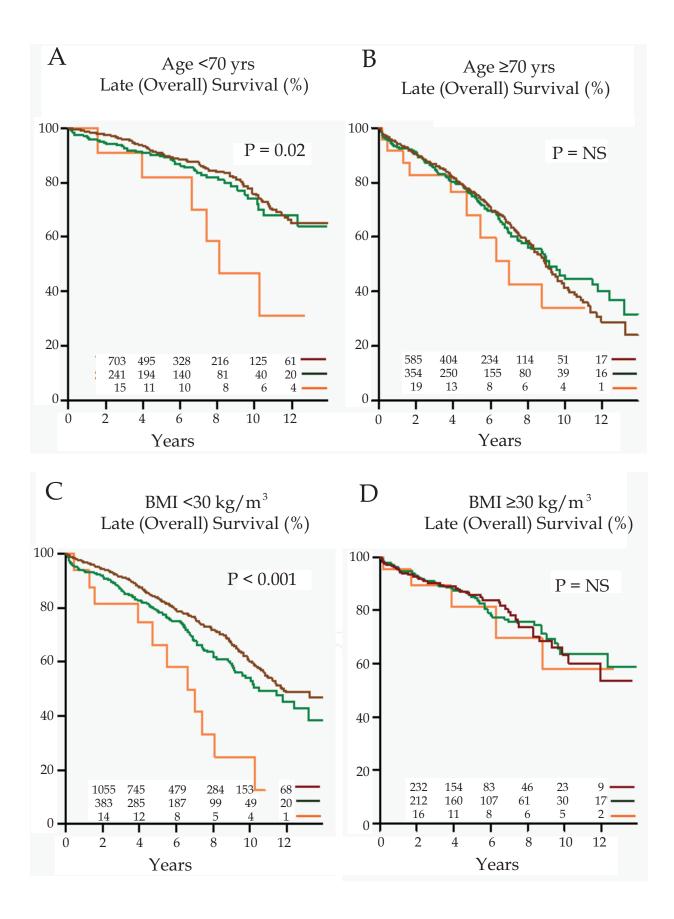


Fig. 5. Freedom from overall mortality in various subdivisions of the three effective orifice area index (EOAI) groups (Jamieson et al., 2010, and Jamieson, Personal Communication). E1 (solid line), not significant; E2 (long-dash line), mild to moderate; and E3 (short-dash line), severe. (EF = ejection fraction; BMI = body mass index)



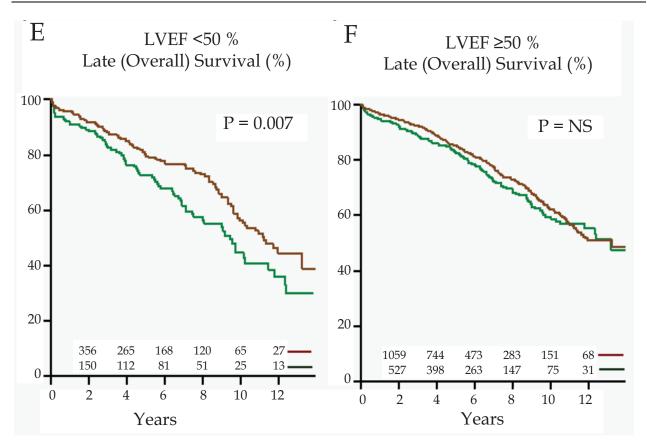


Fig. 6. Impact of prosthesis-patient mismatch on late overall survival (from Mohty et al. 2009, Figure 2). (A) Patients < 70 years old, (B) Patients > 70 years old, (C) Body mass index (BMI) < 30 kg/m², (D) BMI > 30 kg/m², (E) Pre-operative left ventricular ejection fraction (LVEF) < 50%, (F) LVEF > 50%. Brown line indicates nonsignificant prosthesis-patient mismatch (PPM); green line indicates moderate PPM; orange line shows severe PPM

In the Jamieson et al. cohort of 3343 patients, an additional study (Higgins et al., 2011) that evaluated the influence of gender on early, late, and overall survival reported that the predictors of mortality after AVR for aortic stenosis differed between male and female patients. Female gender was a predictor of early mortality while male gender was a predictor of late (but not early or overall) mortality. Male gender increased the risk of late mortality, and a valve size ≤ 21 mm increased the risk of early and overall mortality among male patients only. These differences need to be taken into consideration preoperatively and require consideration during operative management.

The Jamieson et al. analysis indicated that severe PPM identified with an EOAI < $0.65 \text{ cm}^2/\text{m}^2$ is not an independent predictor of early mortality, late mortality, or overall mortality after AVR. These findings have been discussed in perspective with other studies that have and have not provided evidence of PPM as an independent predictor of survival. The independent influence of bioprostheses as a risk factor of late and overall mortality also needs extensive evaluation because currently bioprostheses are recommended for patients \geq 60 years old to minimize serious valve-related morbidity and provide a relatively acceptable degree of valve-related reoperation for structural valve deterioration. Valve-related mortality is not influenced by valve type (bioprosthesis or mechanical prosthesis). The

documented finding that AVR does not provide the same age/gender matched survival as in the general population allows this lower age threshold for bioprostheses in AVR (van Geldrop et al., 2009). This earlier failure threshold may be related to residual systolic dysfunction and more likely related to diastolic dysfunction concomitant with PPM (Nozohoor et al., 2008).

3. A suggested approach to PPM

Because the negative impact of severe PPM on postoperative survival, it is crucial to avoid leaving patients with severe PPM after valvular surgery. Pibarot and Dumesnil (2000) presented a 3-step approach for preventing PPM: [1] calculate the patient's body surface area from weight and height; [2] using a BSA versus EOAI table, find the minimal valve EOA (in cm²) that will allow a given patient to have proper (ideally > 0.85 cm² / m²) EOAI after surgery; and [3] select the type and size of prosthesis that has EOA reference values equal to or greater than the minimal valve EOA value obtained in step 2. The occurrence and severity of postoperative PPM can also be predicted before the operation from the patient's BSA and the reference EOA value of the selected prosthesis (Pibarot et al., 2001; Urso et al., 2010; Dumesnil and Pibarot, 2010).

In agreement with the above, despite failing to find severe PPM (< 0.65 cm² / m²) as an independent predictor of early, late, or overall mortality after AVR, we recommend that surgeons do not leave patients with a severe mismatch (especially for bioprostheses, which may develop degenerative changes over time that would further reduce the EOAI). Surgeons should maintain a prospective strategy of implanting an adequately sized aortic prosthesis that will preclude patients from being in the category of severe mismatch (near equivalent to indications for intervention in severe aortic stenosis). However, a significant portion of patients undergoing AVR will have some level of mild-to-moderate PPM owing to the intrinsic obstructive nature of most prostheses, and Jamieson et al. (2010) should provide some confidence to surgeons and cardiologists that mild-to-moderate PPM is unlikely to be detrimental to survival.

Other than selecting a prosthesis with sufficient EOA, as described above, there are several more intraoperative options available to surgeons to prevent the occurrence of severe PPM. Aortic root enlargement may be considered in patients with an elevated risk of developing moderate-to-severe PPM at time of valvular replacement surgery (Mohty et al., 2006). Kulik et al. (2008) were able to insert larger prosthetic valves and achieve lower PPM by doing aortic root enlargement (ARE) at the time of AVR. They reported that the addition of an ARE to AVR increased the aortic cross-clamp time by 9.9 minutes, on average, and that there was no significant increase in perioperative morbidity or mortality associated with the added ARE. However, the lower incidence of PPM did not significantly affect long-term outcomes in their AVR + ARE cohort, once again coming back to the question of whether PPM significantly affects survival. The third option is a total aortic root replacement. Compared with a traditional stented bioprosthesis, total root replacement allows for optimal hemodynamics with no significant aortic regurgitation, improved regression of the LV mass, and less PPM in the small aortic root (Kon et al., 2002; Kincaid et al., 2007); however, total aortic root replacement comes at the cost of increased operative mortality, and a longer learning process. Several biological valves that allow for this procedure are the Medtronic

Freestyle (porcine, stentless), Edwards Prima Plus (porcine, stentless), and Sorin Pericarbon Freedom (pericardial, stentless) (Jamieson, 2010). Finally, a myectomy and a myotomy of the hypertrophied muscle are options for dealing with a small aortic root or a left ventricular outflow tract obstruction; they are safe and effective procedures without additional complications when done concomitantly with AVR (Kayalar et al., 2010). Myectomy-myotomy also has improved left ventricular mass regression after AVR for pure aortic stenosis (Tasca et al., 2003).

Among the three available intraoperative options available to surgeons to prevent the occurrence of severe PPM, the first option to consider for any patient should be to look for a valve with larger a EOAI and better hemodynamics. The On-X valve and the St. Jude Medical (SJM) Regent valve are mechanical valves with improved hemodynamics. The On-X valve by On-X Life Technologies Inc. also has improved hemodynamics (Palatianos et al., 2007; Chambers et al., 2005) and excellent postoperative EOA and transvalvular gradients (Moidl et al., 2002). The On-X valve was also designed to address the problems of occasional incidents of unexplained hemolytic anemia, tissue interference, excessive pannus overgrowth, and thrombotic complications (Moidl et al., 2002). The SJM Regent valve is an improvement on the SJM conventional valve, and has a wider valve area than the SJM HP valve (Sezai et al., 2010). With its supra-annular placement, several studies have suggested that using the Regent valve practically circumvents the need for root enlargement (Bach et al., 2002; Petracek, 2002). In a recent study (Okamura et al., 2010) in which 50 patients were given a small-sized (17-mm or 19-mm) St. Jude Regent mechanical valve, all patients improved to NYHA functional class II or better. Several biological valves with improved hemodynamics are the Carpentier-Edwards PERIMOUNT Magna Ease (pericardial), SJM Epic Supra (porcine), Sorin Soprano Armania (pericardial), and Medtronic Mosaic Ultra (porcine) valves (Jamieson, 2010). The Sorin Mitroflow (pericardial) and the St Jude Medical Trifecta (pericardial) (approved 2007 and 2010, respectively by the USFDA) are externally mounted pericardial bioprostheses and not amenable to increased diameter design.

For patients who have already developed moderate or severe postoperative PPM, reoperation may be an option to improve long-term survival (Girard et al., 2001). In Girard et al., there were no 30-day deaths for reoperations on 12 patients with isolated, severe PPM. However, 5 of the 9 patients who underwent concomitant major cardiac procedures at the time of valvular replacement died in-hospital, so there is a risk to reoperation. The benefit of relief from PPM must be weighed carefully against the risks of reoperation, and must be assessed on a patient-by-patient basis. When evaluating patients with mild-to-moderate PPM for the possibility of reoperation, we suggest that surgeons take into account the Jamieson et al. (2010) finding of the unlikelihood of mild-to-moderate PPM contributing to worse survival.

From the accumulated data from published literature, it is easy to see that the topic of prosthesis-patient mismatch remains controversial. The issue is further complicated by the fact that there are several levels of PPM (nonsignificant, mild, moderate, or severe), with different studies showing different outcomes for each level of PPM. There is also currently no clear consensus on the exact definitions of PPM and its categories.

A sensible approach to the issue of PPM is that we should avoid generalizations for any given level of PPM except for severe PPM, for which the data in the existing literature is

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more consistent; therefore, proactive measures should be taken to prevent its occurrence. For other levels of PPM, it is reasonable to evaluate each patient on an individual basis (i.e., moderate PPM being more acceptable for a sedentary elderly patient, but less so for someone who is younger and more active), and for surgical and postoperative management options to be dependent on the individualized assessment.

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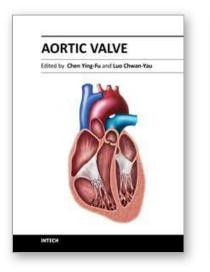
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Aortic Valve Edited by Prof. Chen Ying-Fu

ISBN 978-953-307-561-7 Hard cover, 350 pages **Publisher** InTech **Published online** 09, December, 2011 **Published in print edition** December, 2011

Much has evolved in the field of aortic valve disease because of the increase in knowledge in the last decade, especially in the area of its management. This book "Aortic Valve" is comprised of 18 chapters covering basic science, general consideration of aortic valve disease, infective endocarditis, aortic sclerosis and aortic stenosis, bioprosthetic valve, transcatheter aortic valve implantation and a special section on congenital anomalies of the aortic valve. We hope this book will be particularly useful to cardiologists and cardiovascular surgeons and trainees. We also believe that this book will be a valuable resource for radiologists, pathologists, cardiovascular anesthesiologists, and other healthcare professionals who have a special interest in treating patients with aortic valve disease. We are certain that information in this book will help to provide virtually most new areas of aortic valve disease that will be employed in the current era.

How to reference

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W.R. Eric Jamieson, Charlie Zhang, Jennifer Higgins, Michael H. Yamashita and Jian Ye (2011). Influence of Prosthesis-Patient Mismatch on Survival with Aortic Valve Replacement, Aortic Valve, Prof. Chen Ying-Fu (Ed.), ISBN: 978-953-307-561-7, InTech, Available from: http://www.intechopen.com/books/aortic-valve/influence-of-prosthesis-patient-mismatch-on-survival-with-aortic-valve-replacement



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