The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27 186 patients with 133 141 patient-years


CRD summary
This review concluded that prosthesis-patient mismatch (of artificial heart valves) was associated with an increase in all-cause and cardiac-related mortality over long-term follow-up after aortic valve replacement in adult patients. Although there were potential limitations because of the observational nature of the included evidence, the authors' conclusions are likely to be reliable.

Authors' objectives
To determine the association between prosthesis-patient mismatch and long-term survival after aortic valve replacement in adults.

Searching
MEDLINE and EMBASE databases were searched in January 2011 for published articles in English; search terms were reported. Additional studies were identified from the reference lists of relevant reviews and included studies.

Study selection
Studies were eligible for inclusion if they assessed prosthesis-patient mismatch in adults who had undergone aortic valve replacement with a bioprosthetic or mechanical valve. Studies had to measure long-term survival with a minimum of five years follow-up.

Prospective and retrospective cohort studies were included in the review. The mean age of included patients ranged from 46.5 to 78 years and mean length of follow-up ranged from 2.5 to 10 years. Across all included studies, patients were recruited between 1976 and 2009. Most included studies defined prosthesis-patient mismatch as an indexed effective orifice area of 0.85 cm$^2$/m$^2$ or over.

Studies were selected independently by two researchers.

Assessment of study quality
The authors did not appear to assess study quality.

Data extraction
Two researchers extracted all-cause and cardiac-related mortality as hazard ratios (HR). Where the hazard ratio and corresponding variance were not reported, data was extracted from available Kaplan-Maier survival curves; the number of patients at risk reported for each time frame was used to estimate a logarithmic hazard ratio and related 95% confidence interval (CI). Where these data were unavailable, the method described by Parmar was used. Study authors were contacted for missing information.

Methods of synthesis
Pooled hazard ratios and related 95% confidence intervals were calculated using a random-effects model. Heterogeneity was assessed using $I^2$ and the Q statistic.

Subgroup analyses were conducted to explore differences in valve type, study design, year of publications, location, length of follow-up, patient age and effective orifice area determination. Sensitivity analysis was conducted to assess the impact of year of patient recruitment.

Potential publication bias was assessed using funnel plots.

Results of the review
Thirty-four studies (27,186 patients; 133,141 patient years) were included in the review. Twenty-seven studies (21,802 patients) used the universally accredited indexed effective orifice area of 0.85 cm$^2$/m$^2$ or more, categorising 44.2% of patients as having prosthesis-patient mismatch. Seven studies diagnosed 34.2% of patients with moderate prosthesis-patient mismatch (>0.65 to >0.85 cm$^2$/m$^2$) and 9.8% with severe prosthesis-patient mismatch (<0.65 cm$^2$/m$^2$).

Prosthesis-patient mismatch was associated with a statistically significant increase in all-cause mortality when compared with patients without prosthesis-patient mismatch (HR 1.34, 95% CI 1.18 to 1.51; 18 studies; I$^2$=35%); the increase in cardiac-related mortality was not statistically significant (HR 1.51, 95% CI 0.88 to 2.60; nine studies; I$^2$=67%).

Moderate prosthesis-patient mismatch was associated with statistically greater all-cause mortality (HR 1.19, 95% CI 1.07 to 1.33; 10 studies, I$^2$=26%) and cardiac-related mortality (HR 1.32, 95% CI 1.02 to 1.71; three studies, I$^2$=0%).

Severe prosthesis-patient mismatch was associated with statistically greater all-cause mortality (HR 1.84, 95% CI 1.38 to 2.45; 12 studies; I$^2$=79%) and cardiac-related mortality (HR 6.46, 95% CI 2.79 to 14.97; three studies, I$^2$=42%).

There was a constant hazard over time for all-cause mortality, whereas cardiac-related showed more variation in hazard ratios over time.

Subgroup analyses indicated statistical heterogeneity between studies using bioprosthetic and mechanical valves on all-cause mortality. Sensitivity analyses were reported.

There was no evidence of publication bias.

**Authors' conclusions**

Prosthesis–patient mismatch was associated with an increase in all-cause and cardiac-related mortality over long-term follow-up. Efforts to prevent prosthesis-patient mismatch should receive more emphasis and widespread acceptance to improve long-term survival after aortic valve replacement.

**CRD commentary**

The review question was supported by appropriate inclusion criteria. Adequate efforts were made to identify relevant English language publications. Although relevant non-English language and/or unpublished studies may have been overlooked, the authors did not find obvious evidence to suggest publication bias. Methods designed to reduce reviewer bias and error were used in the study selection and data extraction stages of the review process.

The quality of the included studies was not formally assessed, although the authors noted that the proportion of patients followed-up was often greater than 95% among the included studies; subgroup analyses did not reveal substantially different outcomes for prospective and retrospective designs. In the absence of controlled studies, the inclusion of non-controlled cohort studies appeared appropriate; outcomes from these studies appeared to be pooled using appropriate methods. The authors considered significant subgroup findings to be hypothesis-generating, and restricted their overall conclusions to the main survival analysis.

Despite potential limitations due to the observational nature of the included studies, the authors' conclusions appear to follow from the evidence presented and are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that a strategy to prevent prosthesis-patient mismatch should be implemented at the time of operation by calculating the minimum valve effective orifice area required for the patient to select the appropriate product. The authors also stressed the importance of avoiding prosthesis-patient mismatch in younger patients and those with depressed left ventricular systolic function. The authors recommended that aortic root enlargement should be considered if severe prosthesis-patient mismatch could not be avoided with the use of the available valves.

**Research:** The authors stated that future studies should report data for patients with mechanical and bioprosthetic valves separately. They added that further studies with bigger sample sizes were needed to assess the usefulness of transcatheter aortic valve implantation for the prevention of prosthesis-patient mismatch.

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