Comparison of bioprosthesis and mechanical valves, a meta-analysis of randomised clinical trials

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Authors' objectives
To compare the outcomes of patients who randomly received mechanical valves or bioprosthesis, over a long-term clinical follow-up.

Searching
MEDLINE was searched from 1966 up to and including 1997 using three different search strategies. Pascal Biomed and EMBASE, from 1990 and 1989 respectively, were also searched. References to all comparative randomised and non-randomised clinical trials and reviews were examined. Published short communications and abstracts were identified by inspecting the proceedings of three series of international conferences in cardiology, published annually in: Circulation (from 1975), the Journal of American College of Cardiology (from 1983) and the European Heart Journal (from 1980). Manufacturers of heart valves (St. Jude Medical and MEDTRONIC) and the investigators of all the comparative studies were contacted for unpublished trials.

Study selection
Study designs of evaluations included in the review
Randomised controlled clinical trials (RCTs) comparing bioprosthesis and mechanical prostheses were included.

Specific interventions included in the review
The studies were required to compare bioprostheses and mechanical prostheses in order to be included.

Participants included in the review
The authors did not specify any disease or participant inclusion or exclusion criteria. The participants included in the studies were those undergoing an operation to replace a heart valve.

Outcomes assessed in the review
The authors did not specify any inclusion or exclusion criteria relating to the outcomes. The following outcomes were assessed: in-hospital mortality, reoperation, bleeding, thromboembolism, cardiac death and death from all causes ('all death'), and endocarditis. Death from all causes was defined as a primary outcome.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Whilst no formal assessment of validity was undertaken, methodological quality was taken into consideration.

Data extraction
Two independent reviewers screened and extracted morbidity and mortality outcomes, and length of follow-up, using a standard extraction procedure. The trial authors were contacted to confirm the extracted data. The following categories of data were extracted from each study: author; number of patients; type of valve, i.e. aortic, mitral, or aortic and mitral; gender; age; length and collection of follow-up data; randomisation procedure; incidences of in-hospital mortality, bleeding, thromboembolism, endocarditis, reoperation, cardiac death and death from all causes; definitions used for thromboembolism and bleeding; and the anticoagulation used.
Methods of synthesis
How were the studies combined?
The studies were pooled in a meta-analysis using both fixed-effect and random-effects models. Mechanical valve was chosen as the control group. A relative risk (RR) greater than 1 implied the bioprostheses were superior, whilst a value less than 1 implied the opposite. The results presented were obtained using the logarithm of RR.

How were differences between studies investigated?
Heterogeneity between trials was assessed for each outcome (p<0.10). The association was considered to be statistically significant at a p-value less than 0.05. The interaction between the mitral and the aortic site was investigated by computing the heterogeneity after the data were subgrouped according to valve type. The patients who had combined aortic and mitral valve replacement were considered as an independent group.

Results of the review
Three RCTs were included with a total of 1,229 participants.

The results could only be compared after 5 years for all 3 studies, and after 12 years for 3 of the studies, since the length of follow-up was not identical in all 3 studies.

Reoperation was significantly more frequent in patients with bioprostheses after 11-year follow-up (RR=0.4, 95% CI: 0.28, 0.58, p<0.0001), although statistically-significant heterogeneity was found (p=0.059).

Bleeding was more frequent in patients with mechanical prostheses, both after 5 years (RR=2.5, 95% CI: 1.89, 3.49, p<0.0001) and 11 years (RR=1.65, 95% CI: 1.25, 2.18, p<0.0004) of follow-up. However, the increased risk of bleeding at 11 years was only statistically significant with mechanical prostheses in the aortic position (RR=1.93, 95% CI: 1.36, 2.74, p<0.0002).

Endocarditis was more frequent after 11 years in patients with mechanical prostheses (RR=0.6, 95% CI: 0.3, 0.95, p<0.05), but these results were heterogeneous between mitral and aortic valves.

There were no statistically-significant differences between mechanical prostheses and bioprostheses for all deaths after 5 years (RR=1.16, 95% CI: 0.97, 1.39, p=0.1) and 11 years (RR=0.94, 95% CI: 0.84, 1.06, p=0.32), nor in terms of valve position between the two types of valve prostheses. At 5 years, the RR for all deaths for the mitral site was 1.26 (95% CI: 0.99, 1.62, p=0.06) and 1.25 (95% CI: 0.81, 1.37, p=0.69) for the aortic site. The trend towards higher death rates in the mechanical valve group was probably not related to either the excess of bleeding, since the RR of death from bleeding was 1.33 (95% CI: 0.57, 3.09, p=0.51), or to cardiac death at 5 years (RR=1.15 (95% CI: 0.88, 1.50, p=0.31). At 11 years, the RRs of death were 0.95 (95% CI: 0.81, 1.12, p=0.57) and 0.93 (95% CI: 0.79, 1.10, p=0.41) for the mitral and aortic sites, respectively.

Authors' conclusions
The meta-analysis did not show a difference in long-term mortality between mechanical valves and bioprostheses. It confirmed an increased risk of bleeding with mechanical prostheses in both mitral and aortic positions after five years, and only in the aortic position after 11 years. The risk of reoperation after 11 years was higher with bioprostheses for both positions, but there was a statistically-significant heterogeneity between two of the studies.

CRD commentary
The review question was clearly stated, although there were no predefined inclusion criteria relating to participants and outcomes. The literature search was adequate and identified unpublished literature, but the authors did not provide any search terms or specify if the search was restricted to English language articles only. Whilst there was no formal validity assessment, methodological quality was taken into account since the inclusion criteria for study design stipulated RCTs. Studies were appropriately pooled in both a quantitative and narrative synthesis, and heterogeneity was investigated. Some details explaining the review process were provided, e.g. some categories of data were extracted, whereas others were not, e.g. how decisions were made on the relevance of primary studies. The authors' conclusions appear to follow
from the results presented, but should be treated with caution in view of the limitations highlighted.

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

Practice: The authors did not state any implications for practice.

Research: The authors state that larger randomised trials are needed to support these findings, and a meta-analysis should be conducted on individual records to identify patients most likely to benefit from each type of prosthesis.

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