Homograft implantation techniques in the aortic position: to preserve or replace the aortic root?

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CRD summary
The authors found no significant differences in early mortality between groups undergoing homograft implantation in the aortic position using root replacement or root preserving techniques. The root replacement technique group showed a significantly lower rate of reoperation during long-term follow-up. The authors appropriately consider methodological limitations, and their cautious conclusions correctly reflect the poor-quality studies on this topic.

Authors' objectives
To evaluate differences in early- and long-term outcomes of patients undergoing aortic homograft implantation with either a root replacement (RR) or a root preserving (RP) technique.

Searching
MEDLINE and EMBASE were searched from 1965 to August 2005 without any language restrictions; the key terms were reported. The Cochrane Library was also searched using the terms ‘aortic homograft’ and ‘implantation technique’; search dates were not reported for this database. Manual searches were conducted on bibliographies of material collected by the authors.

Study selection
Study designs of evaluations included in the review
Inclusion criteria were not specified in terms of the study design. All of the included studies were retrospective and non-randomised. The mean duration of follow-up was 12.5 years (range: 6 to 29).

Specific interventions included in the review
Studies of homograft implantation techniques using the total RR technique compared with RP techniques (either subcoronary or inclusion cylinder) in the aortic position were eligible for inclusion.

Participants included in the review
Studies in patients undergoing homograft implantation using either the RR or RP techniques in the aortic position were eligible for inclusion. When several papers reported the same patient data, the most recent paper was included. In the included studies 1,141 (35%) patients underwent RR and 1,864 (63%) patients underwent RP.

Outcomes assessed in the review
Studies that reported comparisons between RR and RP (subcoronary, inclusion cylinder) for early (30 day) mortality and overall reoperation rate at maximum follow-up were eligible for inclusion. Studies that reported a zero in two cells of the critical cross-tabulation tables or no event for both groups were excluded. Studies were also excluded if the outcome of comparison data for both techniques was not reported, or if it was not possible to indirectly calculate this.

How were decisions on the relevance of primary studies made?
Two reviewers searched the literature and critically appraised the studies. Any discrepancies were resolved by consensus.

Assessment of study quality
The quality of each study was assessed by examining patient selection, matching of RR and RP patient groups, and assessment of outcome using a modified Newcastle-Ottawa scale. The studies were rated using an ordinal star scoring scale, with higher scores representing studies of higher quality. A study could be awarded a maximum of 1 star for each numbered item within the selection and exposure categories, and a maximum of 4 stars for the comparability of the two groups. The quality of each study was graded as either level 1 (0 to 4 stars) or level 2 (5 to 9 stars). Two reviewers independently assessed study quality. Any discrepancies were resolved by consensus.
Data extraction
Data were extracted on the number of patients operated on with each technique, number of surgeons performing the procedures, length of maximum follow-up, completeness of follow-up, quality of the study and outcomes. Three reviewers independently extracted the data. Any discrepancies were resolved by consensus.

Methods of synthesis
How were the studies combined?
Early mortality data from individual studies were combined using the Mantel-Haenszel chi-squared method of meta-analysis. The data were analysed using both random-effects and fixed-effect models. The hazard ratio (HR) with 95% confidence interval (CI) was used for time to reoperation; the methods used to estimate the HR were reported in full. Publication bias was assessed using a funnel plot and explored using the methods proposed by Begg and Egger. In addition, the ‘trim and fill’ method was used to adjust for publication bias.

How were differences between studies investigated?
Sensitivity analysis was conducted using subgroup analysis of the following variables: study quality (score of 5 stars or more), year of publication (after 1997), sample size (each of the groups compared contained 50 or more cases), studies comparing RR with subcoronary techniques, and studies not identified as outliers in the funnel plot. Cumulative meta-analysis was used to model the variation between studies. The influence of each study on the overall estimated odds ratio (OR) or HR was assessed using influential meta-analysis, by omitting each of the studies sequentially.

Results of the review
Eleven studies (n=3,005) were included, all were retrospective and non-randomised.

The quality of the included studies was poor to moderate. Three of the 11 studies had a score of less than 5. The remainder of the studies had a quality score ranging from 5 to 7.

Early mortality.
Only 9 included studies reported the incidence of early mortality (RR, n=847; RP, n=1,683). The incidence was greater in the RR group (7%, 59 out of 846) compared with the RP group (3.8%, 63 out of 1,667). The fixed-effect model showed that the RR group had significantly higher early mortality than the RP group (OR 1.6, 95% CI: 1.1, 2.4). There was no difference between groups using the random-effects model (OR 2.6, 95% CI: 0.7, 9.7). However, overall heterogeneity was statistically significant (p<0.001). When outliers were removed from the analysis there were no significant differences between groups for the fixed-effect model.

Cumulative meta-analysis and influential sensitivity analysis showed that the difference in early mortality between the RR and RP groups decreased over time. None of the studies showed a significant influence on the overall OR.

A sensitivity analysis showed that statistically significant heterogeneity remained when studies were subgrouped by study quality (p=0.018), study size (p=0.028), year of publication (p=0.032), or patients undergoing subcoronary technique compared with RR (p<0.001). There was no evidence of publication bias (p=0.113).

Reoperation during follow-up.
All 11 included studies were included in the meta-analysis of reoperation rates (RR, n=1,141; RP, n=1,864). The RR group had a significantly lower reoperation rate than the RP group. The overall 0.53 (95% CI: 0.47, 0.59) when using a fixed-effect model and 0.55 (95% CI: 0.38, 0.80) when using a random-effects model. Statistical heterogeneity was significant (p=0.001). The results did not change significantly with the removal of outliers from the analysis, but heterogeneity was no longer significant.

Cumulative meta-analysis and influential sensitivity analysis showed the CIs of the overall HR becoming less wide over time as more studies were added. None of the studies caused significant changes in the direction of the overall HR estimate.

Heterogeneity between the studies was statistically significant for subgroup analyses of patients undergoing subcoronary
technique in the RP group compared with patients undergoing RR (p<0.001), study quality (p=0.001), study size (p<0.001) and year of publication (p<0.001). There was no evidence of publication bias (p=0.226).

**Authors’ conclusions**
There was no significant difference in early mortality between groups undergoing homograft implantation using either RR or RP techniques in the aortic position. The RR technique group showed a significantly lower rate of reoperation during long-term follow-up.

**CRD commentary**
The inclusion criteria were clear in terms of the intervention and outcomes assessed. Some relevant sources were searched, but it is unclear if attempts were made to minimise language bias or to locate unpublished studies. The authors did assess the possibility of publication bias. Two reviewers independently selected studies, assessed validity and extracted the data, thus reducing the potential for reviewer bias and error. The majority of included studies were retrospective in nature; these are subject to various potential biases, with lower quality studies tending to show larger treatment effects. The results from these studies and any synthesis may not, therefore, be reliable. Studies were combined in a meta-analysis and the authors conducted a subgroup analysis to examine sources of heterogeneity. However, the results for individual studies were reported without supporting data or levels of statistical significance, which means it is not possible to verify the findings reported in the review. Since the characteristics of the participants in the included studies were not described, it may be difficult to generalise the review findings. The authors also indicated that selection bias may be present as the two groups of patients were not comparable for all risk factors, but data were not presented. Details provided highlighted considerable clinical variation, and statistical heterogeneity was also found. The authors appropriately considered the limitations in study design and differences across the studies, consequently their cautious conclusions correctly reflect the poor-quality studies on this topic.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated a need for a controlled trial comparing subcoronary and RR techniques using randomisation techniques, either by the same surgeon or by cooperating surgeons equally skilled in both techniques.

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