Preservation versus non-preservation of mitral valve apparatus during mitral valve replacement: a meta-analysis of 3835 patients

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Abstract

Resection of the chordopapillary apparatus during mitral valve replacement has been associated with a negative impact on survival. Mitral valve replacement with the preservation of the mitral valve apparatus has been associated with better outcomes, but surgeons remain refractory to its use. To determine if there is any real difference in preservation vs non-preservation of mitral valve apparatus during mitral valve replacement in terms of outcomes, we performed a systematic review and meta-analysis using MEDLINE, EMBASE, CENTRAL/CCTR, Scielo, LILACS, Google Scholar and reference lists of relevant articles to search for clinical studies that compared outcomes (30-day mortality, postoperative low cardiac output syndrome or 5-year mortality) between preservation vs non-preservation during mitral valve replacement from 1966 to 2011. The principal summary measures were odds ratios (ORs) with 95% confidence interval and *P*-values (that will be considered statistically significant when <0.05). The ORs were combined across studies using a weighted DerSimonian–Laird random-effects model. The meta-analysis was completed using the software Comprehensive Meta-Analysis version 2 (Biostat Inc., Englewood, NJ, USA). Twenty studies (3 randomized and 17 non-randomized) were identified and included a total of 3835 patients (1918 for mitral valve replacement preservation and 1917 for mitral valve replacement non-preservation). There was significant difference between mitral valve replacement preservation and mitral valve replacement non-preservation groups in the risk of 30-day mortality (OR 0.418, $P < 0.001$), postoperative low cardiac output syndrome (OR 0.299, $P < 0.001$) or 5-year mortality (OR 0.380, $P < 0.001$). No publication bias or important heterogeneity of effects on any outcome was observed. In conclusion, we found evidence that argues in favour of the preservation of mitral valve apparatus during mitral valve replacement.

Keywords: Meta-analysis • Heart valve prosthesis implantation • Chordae tendineae

INTRODUCTION

Rationale

Resection of the chordopapillary apparatus during mitral valve replacement has been associated with a negative impact on survival and, on the contrary, more favourable outcomes have been observed with the use of subvalvular preservation techniques. However, most studies do not have probabilistic samples with sufficient sizes to demonstrate results with good power and/or good confidence intervals, which makes results be seen as not conclusive [1–20].

Our meta-analysis attempts to determine if there is any real difference in preservation vs non-preservation of mitral valve apparatus during mitral valve replacement in terms of outcomes.

Objectives

We performed a meta-analysis of studies to compare preservation (mitral valve replacement with preservation [MVR-P]) with non-preservation (mitral valve replacement with non-preservation [MVR-NP]) of mitral valve apparatus during mitral valve replacement, according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [21].

MATERIALS AND METHODS

Eligibility criteria

Using the population, intervention, comparison, outcome, study (PICOS) strategy, studies were considered if: (i) population

comprised patients undergoing mitral valve replacement; (ii) compared outcomes between MVR-P and MVR-NP; (iii) outcomes studied included 30-day mortality, postoperative low cardiac output syndrome (LCOS) or 5-year mortality; (4) were prospective or retrospective or randomized or non-randomized studies.

Information sources

The following databases were used (from 1966 to 2011): MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL/CCTR), ClinicalTrials.gov, SciELO (Scientific Electronic Library Online), LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde – The Latin American and Caribbean Health Sciences), Google Scholar and reference lists of relevant articles.

Search

We conducted the search using Medical Subject Heading terms 'mitral disease' OR 'mitral stenosis' OR 'mitral regurgitation' OR 'mitral insufficiency' OR 'mitral valve disease' OR 'mitral valve prolapsed' AND 'mitral valve replacement' OR 'mitral valve surgery' OR 'heart valve prosthesis implantation' AND 'preservation of subvalvular apparatus' OR 'preservation of chordae tendineae' OR 'chordal-sparing'.

Study selection

The following steps were done: (i) identification of titles of records through database searching; (ii) removal of duplicates; (iii) screening and selection of abstracts; (iv) assessment for eligibility through full-text articles; (v) final inclusion in study.

One reviewer followed steps 1–3. Two independent reviewers followed step 4 and selected studies. Inclusion or exclusion of studies was unanimously decided. When there was disagreement, a third reviewer took the final decision.

Data items

The endpoint was the odds ratio (OR) for 30-day mortality after MVR-P or MVR-NP. Secondary endpoints were the OR for postoperative LCOS or 5-year mortality.

Data collection process

Two independent reviewers extracted the data. When there was disagreement about data, a third reviewer (the first author) checked the data and took the final decision on it. From each study, we extracted patient characteristics, study design and outcomes (number of events and number of total groups). When possible, actual probabilities of mortality after 5-year following MVR-P or MVR-NP were used to calculate ORs. Alternatively, probabilities of mortality were estimated from published Kaplan–Meier survival curves.

Risk of bias in individual studies

Included studies were assessed for the following characteristics: design (prospective or retrospective), presence of randomization (yes or no), multicenter enrolment (yes or no), characteristics of participants (selection bias), characteristics of personnel (performance bias), outcome assessment (detection bias), incomplete outcome data addressed (attrition bias) and match adjustment (yes or no).

Two independent reviewers assessed the risk of bias. Agreement between the two reviewers was assessed using κ statistics for full-text screening, and rating of relevance and risk of bias. When there was disagreement about the risk of bias, a third reviewer (the first author) checked the data and took the final decision on it.

Summary measures

The principal summary measures were ORs with 95% confidence interval and *P*-values (that will be considered statistically significant when <0.05). The meta-analysis was completed using the software Comprehensive Meta-Analysis version 2 (Biostat Inc., Englewood, NJ, USA).

Synthesis of results

Forest plots were generated for graphical presentations of clinical outcomes and we performed the I^2 test and χ^2 test for the assessment of heterogeneity across the studies [22]. Each study was summarized by the OR for MVR-P compared with MVR-NP. The ORs were combined across studies using a weighted DerSimonian–Laird random-effects model [23]. The model was weighted by the number of events in each study.

Risk of bias across studies

To assess the publication bias, a funnel plot was generated (for each outcome), which was statistically assessed by the Begg and Mazumdar's test [24] and the Egger's test [25].

RESULTS

Study selection

A total of 798 citations were identified, of which 34 studies were potentially relevant and retrieved as full text. Twenty publications fulfilled our eligibility criteria. Interobserver reliability of study relevance was excellent ($\kappa=0.84$). Agreement for decisions related to study validity was very good ($\kappa=0.80$). The search strategy can be seen in Fig. 1.

Study characteristics

The characteristics of each study are shown in Table 1. A total of 3835 patients were studied, with 1918 receiving MVR-P and 1917 receiving MVR-NP, including the years 1988–2010. Of the

Figure 1: Flow diagram of studies included in data search.

20 studies, 7 used posterior or bileaflet preservation; 5 used only bileaflet preservation; 3 used only posterior preservation and 5 did not describe the type of preservation. Twelve studies were about mixed mitral pathology; 3 studies involved only rheumatic mitral disease; 2 were about reoperation; 1 study was about ischaemic mitral disease; 1 was only mitral insufficiency; 1 was not described. The overall internal validity was moderate and is illustrated in Table 2.

Synthesis of results

The OR of the risk of 30-day mortality in the MVR-P group compared with the MVR-NP group in each study is reported in Fig. 2. There was no evidence of important heterogeneity of treatment effect among the studies of death. The overall OR (95% confidence interval) of 30-day mortality showed a statistically significant difference in favour of MVR-P compared with MVR-NP (random-effect model: OR 0.418, $P < 0.001$).

The OR of the risk of postoperative LCOS in the MVR-P group compared with the MVR-NP group in each study is reported in Fig. 3. There was no evidence of important heterogeneity of treatment effect among the studies of death. The overall OR (95% confidence interval) of postoperative LCOS showed a statistically significant difference in favour of MVR-P compared with MVR-NP (random-effect model: OR 0.299, $P < 0.001$).

The OR of the risk of 5-year mortality in the MVR-P group compared with the MVR-NP group in each study is reported in Fig. 4. There was no evidence of important heterogeneity of treatment effect among the studies of death. The overall OR (95% confidence interval) of 5-year mortality showed a statistically significant difference in favour of MVR-P compared with MVR-NP (random-effect model: OR 0.380, $P < 0.001$).

Risk of bias across studies

Funnel plot analysis (Fig. 5) disclosed symmetry around the axis for the treatment effect in all outcomes, which means we probably do not have a publication bias related to these endpoints.

DISCUSSION

Summary of evidence

The results of this meta-analysis demonstrate that there was a statistically significant difference in favour of MVR-P compared with MVR-NP in the OR for 30-day mortality, postoperative LCOS and 5-year mortality, the summary measures being free from the influence of heterogeneity of the effects or publication bias.

Table 1: Study characteristics

Study	MVR-P (n)	Type of mitral valve apparatus preservation	MVR-NP (n)	Mitral pathology
Zakai <i>et al.</i> [1]	90	Posterior/bileaflet	32	Mixed
García-Fuster <i>et al.</i> [2]	410	Posterior/bileaflet	156	Mixed
Muthialu <i>et al.</i> [3]	98	Posterior/bileaflet	262	Mixed
Chowdhury <i>et al.</i> [4]	381	Posterior/bileaflet	70	Mixed
Cingoz <i>et al.</i> [5]	43	Bileaflet	51	Mixed
Kayacioglu <i>et al.</i> [6]	15	Posterior	15	Rheumatic mitral stenosis
Borger <i>et al.</i> [7]	286	Bileaflet	227	Reoperation
Wasir <i>et al.</i> [8]	168	Bileaflet	72	Rheumatic
Kirali <i>et al.</i> [9]	23	Posterior	33	Rheumatic mitral insufficiency
Wu <i>et al.</i> [10]	35	Bileaflet	33	Mixed
Glomer <i>et al.</i> [11]	41	Posterior/bileaflet	219	Mixed
Popovic <i>et al.</i> [12]	6	Bileaflet	6	Mitral insufficiency
Lee <i>et al.</i> [13]	68	NR	318	Mixed
Rao <i>et al.</i> [14]	54	Posterior/bileaflet	187	Reoperation
Straub <i>et al.</i> [15]	42	NR	19	Mixed
David <i>et al.</i> [16]	70	NR	84	NR
Dubiel <i>et al.</i> [17]	7	NR	5	Mixed
Horskotte <i>et al.</i> [18]	50	NR	50	Mixed
Hennein <i>et al.</i> [19]	14	Posterior/bileaflet	55	Mixed
Goor <i>et al.</i> [20]	17	Posterior	23	Ischaemic mitral insufficiency

MVR-P: mitral valve replacement with preservation; MVR-NP: mitral valve replacement without preservation; NR: non-reported.

Table 2: Analysis of bias risk: internal validity

Study	Prospective design	Randomization	Multicenter enrolment	Selection bias	Performance bias	Attrition bias	Detection bias	Match adjustment
Zakai <i>et al.</i> [1]	Yes	No	No	A	B	A	B	Yes
García-Fuster <i>et al.</i> [2]	No	No	No	A	B	A	B	Yes
Muthialu <i>et al.</i> [3]	No	No	No	B	B	A	B	Yes
Chowdhury <i>et al.</i> [4]	Yes	No	No	B	B	A	B	Yes
Cingoz <i>et al.</i> [5]	Yes	No	No	A	B	A	B	Yes
Kayacioglu <i>et al.</i> [6]	Yes	No	No	B	B	A	B	No
Borger <i>et al.</i> [7]	No	No	No	B	B	A	B	No
Wasir <i>et al.</i> [8]	No	No	No	B	B	D	B	No
Kirali <i>et al.</i> [9]	Yes	Yes	No	B	B	B	B	Yes
Wu <i>et al.</i> [10]	Yes	Yes	No	C	B	B	B	Yes
Glomer <i>et al.</i> [11]	No	No	No	C	B	B	B	No
Popovic <i>et al.</i> [12]	Yes	No	No	C	B	A	B	No
Lee <i>et al.</i> [13]	No	No	No	C	B	D	B	No
Rao <i>et al.</i> [14]	No	No	No	B	B	A	B	Yes
Straub <i>et al.</i> [15]	No	No	No	B	B	A	B	No
David <i>et al.</i> [16]	No	No	No	B	B	A	B	Yes
Dubiel <i>et al.</i> [17]	No	No	No	B	B	A	B	Yes
Horskotte <i>et al.</i> [18]	Yes	Yes	No	B	B	A	B	Yes
Hennein <i>et al.</i> [19]	Yes	No	No	B	B	A	B	Yes
Goor <i>et al.</i> [20]	No	No	No	B	B	A	B	No

This was performed by two independent reviewers. The overall bias of the combined studies was considered moderate.

A: low bias risk; B: moderate bias risk; C: high bias risk; D: incomplete reporting.

Considerations about mitral valve replacement with preservation

Despite the fact that existing evidence advocates the preservation of the mitral apparatus, it is not routinely performed. Surgeons are refractory to use preservation techniques because a possible left ventricular outflow obstruction may occur as preserved tissue

impedes with prosthesis function, mainly in patients with septal hypertrophy undergoing anterior leaflet preservation [26]. Despite this aspect, our meta-analysis suggests that surgeons should perform, as much as possible, the preservation of mitral apparatus and use techniques to avoid and/or eliminate the problem of left ventricular outflow obstruction. We demonstrated that patients who underwent MVR-P experienced less risk of postoperative

Figure 2: OR and conclusions plot of 30-day mortality associated with MVR-P vs MVR-NP.

Figure 3: OR and conclusions plot of postoperative LCOS associated with MVR-P vs MVR-NP.

Figure 4: OR and conclusions plot of 5-year mortality associated with MVR-P vs MVR-NP.

Figure 5: Publication bias analysis by a funnel plot for the outcomes.

LCOS. In fact, MVR-P may not only impact left ventricular function, but also right ventricular function and this effect may be of importance as many patients undergoing MVR also suffer from right ventricular dysfunction [27].

Our findings associated with these considerations make us consider that the preservation of chordae tendineae is more important than we assume, so surgeons should pay more attention to this issue and as much as possible preserve the annuloventricular connection to achieve a better maintenance of ventricular geometry, myocardial dynamics, left and right ventricular function and, consequently, better results for patients in early- and long-term follow-up.

Risk of bias and limitations

There are inherent limitations with meta-analyses, including the use of cumulative data from summary estimates. Patient data

were gathered from published data, not from the individual patient follow-up. Access to individual patient data would have enabled us to conduct further subgroup analysis and propensity analysis to account for differences between the treatment groups.

The studies included were of varying design, ranging from prospective randomized to retrospective studies. Only three studies were randomized and there is an important problem of the definition of 'randomized'. All randomized studies did not describe the process of randomization, which makes doubt if the samples are truly randomized. The three studies also did not describe how blind they were (single, double, triple), which can generate significant performance and detection biases. There was a variation in selection criteria used by individual surgeons to allocate patients to each group in each study, and the two groups were not always fully matched for important risk factors. This meta-analysis included data from non-randomized observational studies, which reflects the 'real world', but they are limited by treatment bias, confounders and a tendency to overestimate treatment effects. Patient selection alters outcome and thus makes non-randomized studies obviously less robust.

Another limitation is the heterogeneity of the strategies across the studies. Among the studies used in this meta-analysis, we identified 10 different techniques of bileaflet and/or posterior leaflet preservation. This aspect may influence the results.

Finally, this meta-analysis does not establish whether there is any difference between bileaflet and posterior preservation during mitral valve replacement. This is an issue to be addressed in future individual studies and meta-analyses.

Conclusions

We found evidence that argues in favour of the preservation of the mitral valve apparatus during mitral valve replacement (as much as possible).

Conflict of interest: none declared.

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