The role of valve surgery in infective endocarditis management: a systematic review of observational studies that included propensity score analysis


CRD summary
This review evaluated the role of valve surgery in infective endocarditis and found conflicting evidence for a reduction in all-cause mortality, which did not support the current American Heart Association guidelines. The review was generally well-conducted, but the reliability of the authors’ conclusions is unclear.

Authors' objectives
To evaluate the role of valve surgery in infective endocarditis.

Searching
MEDLINE, Web of Science, Zetoc, and ArticleFirst were searched from inception to June 2007 for publications in any language. Search terms were reported.

Study selection
Cohort studies, which compared valve surgery plus antimicrobial therapy with antimicrobial therapy alone, for adult patients (over 16 years) with infective endocarditis, were eligible for inclusion if they used propensity score analysis to adjust for selection bias. The only eligible outcome was mortality, which in the selected studies was in-hospital, six-month and five-year, all-cause mortalities. The included studies were in both multi-centre (including multinational) and single-hospital cohorts of patients with native valve endocarditis, prosthetic valve endocarditis, or both. The proportion of infective endocarditis patients undergoing valve surgery ranged from 28.9% to 41.7% for prosthetic and 20.8% to 49.3% for native valves and the timing of valve surgery was either during initial hospitalisation, with 30 or 31 days of hospitalisation, or not recorded. No details of the age range or sex of patients were given.

The authors did not state how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed independently by two reviewers using the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies with the following validity characteristics: subject selection, group comparability, and outcome. The authors additionally assessed: survivor treatment selection bias; whether the study sample was representative of the infective endocarditis patient population (i.e. whether multi-centre studies controlled for referral bias); whether the patients were recruited in 1990 or later and so were contemporary; adequacy of primary outcome; and loss to follow-up. The validity of the propensity analysis was also assessed for both nonparsimonious model and confounder balance. Details of prognostic factors, which could contribute to a nonparsimonious model, were given.

Data extraction
A structured form was used to extract patient characteristics, including setting, sample size, proportion of cases undergoing valve surgery, mortality data, propensity score and regression analysis variables, and risk estimates, which included relative risk (RR), hazard ratio (HR), and odds ratio, with 95% confidence interval (CI).

Two reviewers independently extracted data with disagreements resolved by consensus.

Methods of synthesis
The synthesis was narrative as the authors considered that the majority of the included studies had certain limitations, which were discussed in detail. The studies were synthesised by outcome and patient type.

Results of the review
Six relevant cohort studies were identified (3,409 patients; range 60 to 1,516). These were published between 1983 and
2007 and included three studies of native valve patients, one study of prosthetic valve patients and two studies of both left-sided native and prosthetic valve endocarditis patients. The authors considered that all six studies suffered from at least one type of bias which could seriously affect their results. The main limitations were inadequate proof of comparability between the intervention and control groups (three studies) and susceptibility to survivor treatment bias (five studies). Three studies were considered to be representative of the infective endocarditis population and two studies contained a nonparsimonious propensity model.

Two cohort studies of patients with native valves found a significant decrease in mortality with valve surgery (HR: 0.4, 95% CI: 0.18 to 0.91, mortality at six months; RR: 0.3 (95% CI: 0.18 to 0.49, in-hospital mortality). A third cohort study of both native and prosthetic valve endocarditis patients also found a significant decrease in mortality at five years (HR: 0.27, 95% CI: 0.13 to 0.55). Two of the remaining studies of in-hospital mortality in prosthetic valve patients and in-hospital mortality in native valve patients also indicated a decrease in mortality with surgery, but the results were not significant.

The study on left-sided native and prosthetic valve patients found a non significant increase in mortality at six months in valve surgery patients. Four subgroups were analysed: left-sided prosthetic valve patients, left-sided native valve patients, complicated left-sided native valve patients, and all patients with further adjustment. All subgroups had non significant increases in mortality at six months.

**Authors’ conclusions**

There was a lack of comparability in the observational studies. These limitations precluded the drawing of firm conclusions and did not provide high quality evidence to support the current American Heart Association guidelines for valve surgery in the management of certain subgroups of infective endocarditis patients. Instead the evidence was conflicting and efficacy was less well-established. Well-designed prospective studies were needed to address the limitations of the available evidence and care is needed when making management decisions in complicated left-sided infective endocarditis.

**CRD commentary**

The review addressed a well-defined question in terms of participants, interventions, study design, and relevant outcomes. Relevant databases were searched, but the authors did not mention whether the reference lists were reviewed or whether unpublished studies were considered. Publication bias was not assessed. Study quality was assessed using suitable criteria and was discussed at length in the paper, but no overall study quality grades were reported. The authors did not state how the papers were selected for the review or how many reviewers performed the selection. Two reviewers independently extracted data with disagreements resolved by consensus and two reviewers assessed study quality but it was not stated in this case how disagreements were resolved. Overall reviewer bias and error therefore could not be ruled out. Some details of the study participants were not extracted, for example their age and sex, and some study details were not reported, for example loss to follow-up. The authors considered that the included studies had certain limitations and therefore provided a narrative synthesis.

The review was generally well-conducted, but due to the limited evidence available, the reliability of the authors’ conclusions was not clear.

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

Practice: The authors stated that although the practice of valve surgery for infective endocarditis management should not be changed, careful scrutiny was required when making management decisions in complicated left-sided infective endocarditis. The evidence did not support the American Heart Association level 1B recommendation for valve surgery in infective endocarditis management.

Research: The authors stated that randomised trials were unlikely to be carried out to examine the impact of surgery on infective endocarditis because the disease is heterogeneous and uncommon. The expert opinion supported surgery, which would make surgeons unwilling to participate and ethical committees unwilling to support a trial. Well-designed observational studies were advocated, with multi-centre, prospective cohorts, representative of the infective endocarditis population, and large enough for subgroup analyses, particularly for prosthetic and native valves. They also
recommended that the evaluation of patients should include transoesophageal echocardiography and detailed and comprehensive data should be gathered, including the timing of different events. The authors also advocated the use of an instrumental variable with a multifaceted analytical approach to address the role of surgery in infective endocarditis.

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