Adverse effects associated with transcatheter aortic valve implantation: a meta-analysis of contemporary studies


CRD summary
Transcatheter aortic valve implantation increased the risk of adverse effects, such as heart block, vascular complications, and renal failure, and the risks differed with the type of valve and route of implantation. There was potential for bias and the mainly observational data were of uncertain quality. The conclusions should be considered tentative pending the results of clinical trials.

Authors' objectives
To determine the adverse effects of transcatheter aortic valve implantation, in patients with severe symptomatic aortic stenosis, at high operative risk. Also, to evaluate whether the type of transcatheter valve and route of valve implantation were associated with differences in adverse effects.

Searching
PubMed was searched up to May 2012, for relevant studies in English; the search terms and strategy were reported. The references of identified articles were screened for additional relevant data.

Study selection
All studies were eligible for inclusion if they included at least 100 patients receiving transcatheter aortic valve implantation, and reported more than one adverse effect. Adverse effects were stroke, vascular complications, implantation of a permanent pacemaker due to heart block, acute renal failure requiring renal replacement therapy, postprocedural moderate-to-severe aortic regurgitation, transcatheter valve embolisation, myocardial infarction, coronary obstruction, multiple transcatheter implantations, and conversion to open heart valve replacement.

The included studies recruited patients between 2005 and 2011. The mean age of patients was 82 years, and 47% of patients were male. Most of the procedures were performed with the Sapien valve or the third-generation CoreValve, which were implanted transarterially or transapically. The mean predicted risk score for operative mortality (measured using the logistic European System for Cardiac Operative Risk Evaluation Score) was 24, indicating high-risk patients. The inclusion and exclusion criteria varied across studies. Most of them reported the adverse effects at 30 days; 30-day and one-year survival were reported.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
Two reviewers independently extracted the rates of adverse effects. Primary study authors were contacted to obtain further information where necessary.

Where data were unavailable, if more than 90% of procedures, in the study, used a given valve type or access route, then all procedures were analysed as part of that subgroup.

Methods of synthesis
A random-effects model, with a restricted maximum likelihood estimator, was used to combine the rates of adverse effects and their 95% confidence intervals. Heterogeneity was assessed using $\chi^2$ and $I^2$. As the data were not normally distributed, they were transformed using arcsine transformation and then back-transformed.

Subgroup analyses were performed by type of transcatheter aortic valve (Sapien or CoreValve) and access route (transarterial or transapical) for the Sapien valve. A mixed-effects linear model was used to assess the effects of
adjusting for different risk profiles (measured using the logistic European System for Cardiac Operative Risk Evaluation Score) on the 30-day and one-year survival rates, for patients who had transcatheter aortic valve implantation performed via the transapical route versus the transarterial route. Sensitivity analysis was performed by excluding national registry data.

Results of the review

Forty-nine studies (16,063 patients) were included in the review. Two were randomised controlled trials (RCTs) comparing transcatheter aortic valve implantation versus medical therapy or aortic valve replacement. Forty-seven studies were observational studies, with over half conducted in single centres.

The overall 30-day survival rate was 91.9% (95% CI 91.1 to 92.8; 49 studies), with significant statistical heterogeneity ($I^2=70.6\%$). The overall one-year survival rate was 79.2% (95% CI 76.9 to 81.4; 38 studies), with significant statistical heterogeneity ($I^2=88.8\%$).

The most frequent adverse effect was permanent pacemaker implantation for heart block, occurring in 13.1% (95% CI 10.3 to 16.3; 44 studies) of patients after transcatheter aortic valve implantation. The overall rate of vascular complications was 10.4% (95% CI 8.0 to 13.1; 36 studies). The overall rate of early stroke was relatively low at 2.9% (95% CI 2.4 to 3.4; 46 studies). All outcomes showed significant statistical heterogeneity.

Other rates of adverse effects were relatively low, including renal replacement therapy (4.9%; 29 studies), moderate-to-severe aortic regurgitation (4.5%; 40 studies), valve embolisation (1.3%; 26 studies), myocardial infarction (1.1%; 37 studies), coronary obstruction (0.8%; 21 studies), valve-in-valve implantation (2.2%; 33 studies), and conversion to open surgery (1.2%; 32 studies). For most outcomes, statistical heterogeneity was greater than 50%.

Subgroup analyses indicated statistically significant differences in survival, rates of vascular complications, and the need for renal replacement therapy, by access route. Pacemaker implantation rates and vascular complications differed significantly by type of transcatheter valve. Further results were reported. Sensitivity analyses did not significantly alter the findings.

Authors’ conclusions

Transcatheter aortic valve implantation was associated with a risk of several important complications, such as heart block, vascular complications, and renal failure. The type of valve and the route of implantation had differing risks of some adverse effects.

CRD commentary

The review question was clearly defined and was supported by fairly broad inclusion criteria. One electronic database was searched and the search was restricted by language, which means that potentially relevant data might have been missed. Data extraction was performed in duplicate, but it was unclear whether this was true for study selection, and reviewer error and bias cannot be ruled out. No quality assessment appears to have been undertaken. The extent that any bias might have affected the results remains unclear, but most studies were observational, introducing a high risk of bias.

Appropriate methods appear to have been used to combine the data, but there was evidence of significant statistical heterogeneity for most outcomes, and the comparisons between different types of valves and access routes were indirect. The authors highlighted some of the limitations of the included studies, including the use of observational data; differing definitions of vascular complications, stroke, and myocardial infarction; and the lack of long-term outcome data. They also highlighted the potential for double counting of patients.

The authors’ conclusions reflect the large amount of evidence, but the potential for bias in the review, and the limitations of this evidence, suggest that these conclusions should be considered tentative pending the results of clinical trials.

Implications of the review for practice and research

Practice: The authors stated that the results should enable clinicians and decision makers to better understand and assess the risks and benefits of valve implantation for patients with severe aortic stenosis.
Research: The authors stated that clinical trials directly comparing the outcomes with different transcatheter valves and different implantation routes were needed.

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