

Influence of Prosthesis Type on Long-Term Survival after Re-replacement of Aortic Valve Prosthesis

Payam Akhyari, MD, Artur Lichtenberg, PhD, Alexander Hartmann, MD, Issam Ismail, MD, Kamiya Hiroyuki, MD, Jan-Philipp Minol, MD, Theodoros Kofidis, PhD, Uwe Klima, PhD, Matthias Karck, PhD, Axel Haverich, PhD

Department of Cardiothoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany



Dr. Akhyari

ABSTRACT

Background: The purpose of this study is to examine the influence of the prosthesis type on early mortality and long-term survival after re-replacement of aortic valve prosthesis, especially in patients over 60 years old.

Methods: Late outcome of 223 patients who underwent a reoperation on the aortic valve and received a mechanical (mechanical group) or biological (biological group) heart valve prosthesis at a single institution were analyzed for survival and major valve-related complications, including structural valve deterioration, thromboembolism, hemorrhage, further reoperation, and valve-related mortality.

Results: Preoperative New York Heart Association class IV ($P = 0.001$), emergency procedure ($P = 0.002$), and endocarditis ($P = 0.025$) were significant risk factors for 30-day mortality rates, which were 8.4 % and 12.5 %, respectively (mechanical versus biological group, $P = 0.361$). A subanalysis of elective patients revealed a low risk of 30-day mortality of 2.4 % and 1.8 %, respectively. Event-free survival was comparable at 5 years ($73.9\% \pm 3.6\%$ versus $70.5\% \pm 6.5\%$, mechanical versus biological group) and 10 year ($49.7\% \pm 5.0\%$ versus $35.3\% \pm 9.8\%$, mechanical versus biological group). In a propensity-matched subanalysis, survival and event-free survival were comparable at 5 and 10 years in both groups.

Conclusion: The type of aortic valve prosthesis did not affect early outcome and late survival in patients who underwent valve replacement, and therefore, the current strategy favoring a biological aortic valve prosthesis for patients aged over 60 years in first-time operations could also be applied in re-replacement.

INTRODUCTION

Aortic valve replacement with a mechanical or biological prosthesis is a standard procedure in cardiac surgery, and as a consequence, reoperative aortic valve replacement has become an increasingly common challenge. Regarding first-time aortic valve replacement, there have been numerous reports on long-term survival and choice of the type of prosthesis (biological or mechanical) [Aupart 2006; Bernet 2007; Khan 2001; Kulik 2006; Lund 2006; Melby 2007; Ruel 2007]. There has been a trend toward a biological prosthesis in the aortic position because of the lower incidence of thrombotic and hemorrhagic complications [Gummert 2005]. Additionally, in older patients a higher durability of biological prostheses has been demonstrated, favoring their implantation [Rahimtoola 2003]. Based on accumulated published evidence and our own experience, in our institution patients over 60 years old have been considered to receive a biological prosthesis as first-time aortic valve replacement. However, to date limited data are available for the reoperative replacement of the aortic valve [Davierwala 2006; Lau 2006; Potter 2005; Vogt 2000] and it remains unclear which strategy should be applied in patients requiring aortic valve re-replacement.

The purpose of this study was to examine the influence of the prosthesis type on early mortality and long-term survival after re-replacement of aortic valve prostheses, especially in patients over 60 years old.

METHODS

Patient Cohort

From 1992 to 2000, 223 patients underwent aortic valve re-replacement at the Hanover Medical School because of dysfunction of a prosthesis or prosthesis endocarditis. All patients were included in the present study. For re-replacement of the aortic valve, 167 patients received a mechanical prosthesis (mechanical group) and 56 patients received a biological prosthesis (biological group), and analyses in the present study were done according to this categorization. Patients having multiple replacement procedures with third-time (or further) operations were excluded from this study. Preoperative, perioperative, and postoperative data were entered prospectively into a computerized database. The patients were evaluated by telephone

Received June 27, 2010; accepted May 15, 2012.

Correspondence: Payam Akhyari, MD, Department of Cardiovascular Surgery, Duesseldorf University Hospital, Moorenstrasse 5, 40225 Duesseldorf, Germany; 0049-211-81-18331 (e-mail: payam.akhyari@med.uni-duesseldorf.de).

interviews, and health records and consultations were evaluated when appropriate. Follow-up periods were an average of 6.4 ± 3.7 years (mechanical group) and 5.1 ± 3.3 years (biological group) after initial operation. Follow-up was 91.5 % complete (151 patients with mechanical prosthesis and 53 patients with biological prosthesis). The end points compared were survival and major valve-related complications, including structural valve deterioration, thromboembolism, hemorrhage, further reoperation, and valve-related mortality. Valve-related mortality included death caused by structural valve deterioration, nonstructural dysfunction, thrombosis, thromboembolism, hemorrhage, or prosthetic valve endocarditis and death related to reoperation for a valve-related complication. Valve-related mortality was inclusive of sudden, unexplained, unexpected deaths. Valve-related morbidity included permanent valve-related impairment as a result of permanent neurologic or other functional deficit caused by structural valve deterioration, nonstructural valve dysfunction, valve thrombosis, thrombotic embolism, bleeding, prosthetic valve endocarditis, or reoperation. The publication Guidelines for Reporting Morbidity and Mortality after Cardiac Valvular Operations [Edmunds1996] was used to define the complications. This retrospective study was approved by our institutional ethics board.

Statistical Analysis

Results are expressed as mean $\pm$ standard deviation. Statistical analyses were performed using the Student's *t*-test for continuous variables or χ^2 tests (Fisher's exact tests if $n < 5$) for categorical variables. Stepwise multivariable logistic regression analysis was used to calculate risk-adjusted odds ratios and to determine the independent predictors of 30-day mortality. Kaplan-Meier analysis was used to compare late mortality between the subject groups. A propensity score-matching analysis was used to compensate for the differences in patient characteristics. For this purpose, logistic regression was used to develop a propensity score [Blackstone 2002]. The propensity score included age, sex, left ventricular ejection fraction (EF), emergency procedure, endocarditis, and New York Heart Association (NYHA) class IV. By using these covariables, a propensity score was calculated for each patient. Finally, each patient in the biological group was matched to 1 patient in the mechanical group with the closest propensity score. The maximum difference of propensity score for a match was $>.015$. By using this novel method, comparable patient groups, 27 patients from each group, were identified for final analysis. A *P* value of <0.05 was considered significant. All statistical analyses were performed using SPSS 12.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Preoperative characteristics and demographics of the study patients are summarized in Table 1. Patients who received a biological prosthesis were significantly older, and the duration from the first operation until the re-replacement of the aortic prosthesis was significantly longer in patients who received a mechanical prosthesis. There were no other differences in preoperative characteristics between the 2 groups.

Operative Procedures

Details of operative procedures are summarized in Table 1. The size of the valve prosthesis was 24.0 ± 2.3 mm in the mechanical group and 23.6 ± 1.7 mm in the biological group ($P = 0.243$). Concomitant surgical procedures were performed in 79 patients (35.4 %) in the entire study cohort, 62 patients (37.1 %) in the mechanical group, and 17 patients (30.4 %) in the biological group ($P = 0.359$). The variety of concomitant surgical procedures was similar between groups; no significant differences of cross-clamp times were observed among the 2 groups.

Early Outcome

Postoperative mortality and complications are listed in Table 2. Thirty-day mortality was 8.4% ($n = 14$) in the mechanical group and 12.5 % ($n = 7$) in the biological group ($P = 0.361$). There were no significant differences in the incidence of postoperative complications between both groups. The results of multivariate analysis for predictors of 30-day mortality are listed in Table 3. In this analysis, preoperative critical condition with NYHA class IV ($P = 0.001$), emergency procedure ($P = 0.002$), and endocarditis ($P = 0.025$) were significant risk factors. Likewise, when patients with endocarditis or NYHA class IV were excluded from further analysis, the 30-day mortality was 2.4 % ($n = 4$) in the mechanical group and 1.8 % ($n = 1$) in the biological group. There was a trend toward higher mortality rates in patients who underwent concomitant coronary artery bypass grafting (CABG). Importantly, there was no influence of valve type on early mortality.

Late Outcome

Death after postoperative day 30 occurred in 40 patients (valve related, 22; non-valve related, 13; unknown, 5) in the mechanical group and 12 patients (valve related, 5; non-valve related, 4; unknown, 3) in the biological group. The result of survival analysis in the entire study cohort is demonstrated in Figure 1A. Survival at 5 years was $77.2\% \pm 3.4\%$ in the mechanical group and $81.0\% \pm 5.4\%$ in the biological group, and survival at 10 years was $59.0\% \pm 4.9\%$ in the mechanical group and $43.9\% \pm 10.6\%$ in the biological group. There was no significant difference in late survival between the 2 groups. Valve-related morbidity occurred in 13 patients in the mechanical group and 6 patients in the biological group. The result of event-free survival (without death and valve-related morbidity) is demonstrated in Figure 1B. Event-free survival at 5 years was $73.9\% \pm 3.6\%$ in the mechanical group and $70.5\% \pm 6.5\%$ in the biological group, with 10-year rates of $49.7\% \pm 5.0\%$ in the mechanical group and $35.3\% \pm 9.8\%$ in the biological group. Interestingly, there was no significant difference between groups.

To focus on the primary interest of this study, patients in the biological group aged over 60 years were 1:1 matched with propensity score according to the following parameters: age, sex, EF, emergency procedure, endocarditis, and NYHA class IV. From each group, 27 patients were matched for further evaluation. All of the matched patients in the biological group and 25 (93%) patients in the mechanical group had late follow-up data. Thus, 25 matched patients in the mechanical

Table 1. Preoperative Characteristics and Operative Procedures*

	Mechanical (n = 167)	Biological (n = 56)	P
Age, years	58.8 ± 13.3	64.6 ± 15.1	0.011
Male, %	117 (70.0)	38 (67.9)	0.741
Body mass index	24.9 ± 3.3	24.7 ± 3.1	0.704
Hypertension, %	74 (44.3)	24 (42.9)	0.877
Hypercholesterolemia, %	35 (21.0)	13 (23.2)	0.711
Current smoking, %	11 (6.6)	3 (5.4)	0.999
Diabetes mellitus, %	13 (7.8)	7 (12.5)	0.288
Dialysis, %	5 (3.0)	3 (5.4)	0.418
Peripheral vascular disease, %	14 (20.9)	4 (7.1)	0.443
Chronic obstructive pulmonary disease, %	14 (20.9)	5 (8.9)	0.899
EF, %	55.2 ± 16.1	56.8 ± 14.9	0.616
Previous myocardial infarction	11 (6.6)	5 (8.9)	0.556
NYHA status	3.0 ± 0.6	3.0 ± 0.6	0.853
Emergency procedure, %	8 (4.8)	6 (10.7)	0.122
Endocarditis, %	17 (10.2)	8 (14.3)	0.399
Time from the previous operation, years	9.1 ± 5.1	7.0 ± 5.1	0.009
Size of aortic valve prosthesis, mm	24.0 ± 2.3	23.6 ± 1.7	0.243
Cross-clamp time, min	86.8 ± 34.7	90.1 ± 33.0	0.535
Concomitant surgery, %	102 (61.1)	30 (53.6)	0.323
CABG, %	27 (16.2)	12 (21.4)	0.370
Aortic root replacement	42 (25.1)	12 (21.4)	0.559
Ascending aorta replacement	15 (9.0)	7 (12.5)	0.453
Mitral valve surgery, %	19 (11.4)	5 (8.9)	0.609
Tricuspid valve surgery, %	15 (9.0)	6 (10.7)	0.701

*Values are mean (SD) or number (%).

group and 27 matched patients in the biological group were analyzed for long-term outcomes. The results of survival analysis and event-free survival in the matched study cohort are shown in Figure 1C and D. In this cohort, survival at 5 years was 67.1% ± 9.6% in the mechanical group and 77.6% ± 8.1% in the biological group, and survival at 10 years was 43.6% ± 12.8% in the mechanical group and 30% ± 15.5% in the biological group. Event-free survival at 5 years was 63.8% ± 9.7% and 70% ± 8.9%, respectively, and event-free survival at 10 years was 26.5% ± 12.1% and 18.2% ± 14.7%, respectively. There were no significant differences between these 2 groups in each analysis.

DISCUSSION

The crucial findings of our study are as follows. (1) In our total series, re-replacement of an aortic valve prosthesis was still a high-risk procedure, with a 9.4% overall mortality rate at 30 days. Decreased patient status with NYHA class IV ($P = 0.001$), emergency procedure ($P = 0.002$), and endocarditis ($P = 0.025$) were significant risk factors diminishing the

long-term results, and for concomitant CABG procedures there was a strong trend toward a risk factor, although statistical significance was not reached ($P = 0.06$). Moreover, the type of aortic valve prosthesis did not have an influence on early outcome. (2) Similarly, in the long term, the type of the aortic valve prosthesis did not significantly influence overall survival or event-free survival. In the matched patient cohort over 60 years old, the late survival rates and event-free survival rates were almost identical in both groups.

As speculated, there was no influence of the type of aortic valve prosthesis on any of the examined variables determining early outcome. The risk factors for early mortality as detected in our analysis support previous findings [Davierwala 2006; Potter 2005; Vogt 2000]. Peripheral vascular disease, prosthetic endocarditis, worsening NYHA class, and need for an aortic annular enlargement were demonstrated as significant risk factors for early mortality in reported series by Davierwala et al, with 216 patients undergoing re-replacement of an aortic valve prosthesis [Davierwala 2006]. Similar results were presented by Vogt et al in their series including 172 patients [Vogt 2000] and by Potter et al with 162 patients [Potter

Table 2. Postoperative Complications*

	Mechanical (n = 167)	Biological (n = 56)	P
Overall 30-day mortality	14 (8.4)	7 (12.5)	0.361
30-Day mortality without endocarditis or NYHA IV	4 (3.2)	1 (2.9)	0.924
Re-thoracotomy for bleeding	14 (8.4)	6 (10.7)	0.579
New onset of renal insufficiency with dialysis	5 (3.0)	4 (7.1)	0.228
Myocardial infarction	3 (1.8)	1 (1.8)	0.999
Low output syndrome	11 (6.6)	3 (0)	0.999
Neurological complication	19 (11.4)	9 (1.8)	0.359
Permanent/stroke	8 (4.8)	5 (8.9)	0.253
Temporal	16 (9.6)	4 (7.1)	0.788
Pneumonia	6 (3.6)	1 (1.8)	0.682

*Values are number (%).

Table 3. Predictive Risk Factors*

	Odds Ratio	95% Confidence Interval	P
Age	1.034	0.985-1.086	0.171
Sex	0.932	0.323-2.684	0.896
Valve type	1.175	0.379-3.644	0.780
NYHA class IV	11.304	4.126-30.971	0.001
Emergency procedure	6.701	2.006-22.309	0.002
Endocarditis	3.107	1.153-8.372	0.025
Concomitant CABG	7.814	0.919-66.482	0.060

*Baseline assumptions for dichotomous variables: Sex, male; valve type, biological; NYHA class IV; concomitant CABG.

2005]. Those previous large series demonstrated that the type of prosthesis did not influence early outcomes, results similar to those of our present study.

However, reports evaluating the late outcome after a re-replacement of the aortic valve prosthesis are very limited. Lau et al. analyzed the long-term outcome of 298 patients who had successful aortic valve re-replacement [Lau 2006]. In their analysis, no significant differences in the survival rates between the 2 valve types were observed in patients older than 60 years, and overall freedom from valve-specific complications and valve-related mortality did not significantly differ between the 2 groups. The results of the present study support their findings. In our entire study cohort, no significant differences in survival and event-free survival were found. In a matched patient cohort with an age of more than 60 years, survival- and event-free survival curves were almost identical between the 2 groups of patients with a biological or a mechanical prosthesis. Although biological prostheses had no advantage for event-free survival in this patient cohort, we consider that biological prostheses may be advisable for patients aged over 60 years requiring re-replacement of an in situ aortic valve prosthesis because of the better quality of life without anticoagulation.

On the basis of this amount of evidence, the question arises whether the operative strategy regarding the choice of prosthesis type at the time of a redo procedure should differ from that used in the first-time operation. Khan et al. have analyzed 1389 patients undergoing first-time replacement of the aortic valve. Comparing late outcomes of tissue and mechanical prosthesis in patients aged over 65 years, they reported survival rates of $71\% \pm 2.2\%$ in the tissue valve group and $71\% \pm 2.4\%$ in the mechanical valve group at 5 years, corresponding to 10-year survival rates of $40\% \pm 3.2\%$ and $39\% \pm 3.1\%$, respectively [Khan 2001]. Their results are similar to those demonstrated in the present study. Accordingly, in a review article by Rahimtoola in 2002, it was emphasized that the use of a biological prosthesis for aortic valve replacement could be advisable for patients aged over 60 to 65 years [Rahimtoola 2003]. The results of the present study suggest that the same strategy regarding consideration of patient age in the choice of the type of prosthesis used in first-time operations can also be used in re-replacement of the aortic valve prosthesis.

In summary, the type of aortic valve prosthesis did not affect early outcome and late survival in patients who underwent replacement. In matched patient cohorts aged over 60

years, late survival and event-free survival were almost identical in both groups. These results suggest that the current strategy favoring the use of biological aortic valve prostheses for patients aged over 60 years in first-time operations could also be applied in re-replacement operations.

REFERENCES

- Aupart MR, Mirza A, Meurisse YA, et al. 2006. Perimount pericardial bioprosthesis for aortic calcified stenosis: 18-year experience with 1133 patients. *J Heart Valve Dis* 15: 768-75.
- Bernet FH, Baykut D, Grize L, et al. 2007. Single-center outcome analysis of 1,161 patients with St. Jude Medical and ATS open pivot mechanical heart valves. *J Heart Valve Dis* 16:151-8.
- Blackstone EH. 2002. Comparing apples and oranges. *J Thorac Cardiovasc Surg* 123:8-15.
- Davierwala PM, Borger MA, David TE, et al. 2006. Reoperation is not an independent predictor of mortality during aortic valve surgery. *J Thorac Cardiovasc Surg*. 131:329-35.
- Edmunds LH Jr, Clark RE, Cohn LH, et al. 1996. Guidelines for reporting morbidity and mortality after cardiac valvular operations. The American Association for Thoracic Surgery, Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity. *Ann Thorac Surg* 62:932-5.
- Gummert JF, Funkat A, Krian A, et al. 2004. Cardiac surgery in Germany during 2004: a report on behalf of the German Society for Thoracic and Cardiovascular Surgery. *Thorac Cardiovasc Surg* 53:391-9.
- Khan SS, Trento A, DeRobertis RN, et al. 2001. Twenty-year comparison of tissue and mechanical valve replacement. *J Thorac Cardiovasc Surg* 122:257-69.
- Kulik A, Bédard P, Lam BK, et al. 2006. Mechanical versus bioprosthetic valve replacement in middle-aged patients. *Eur J Cardiothorac Surg* 30:485-91.
- Lau L, Jamieson WR, Hughes C, et al. 2006. What prosthesis should be used at valve re-replacement after structural valve deterioration of a bioprosthesis? *Ann Thorac Surg* 82:2123-32.
- Lund O, Bland M. 2006. Risk-corrected impact of mechanical versus bioprosthetic valves on long-term mortality after aortic valve replacement. *J Thorac Cardiovasc Surg*. 132:20-6.
- Melby SJ, Zierer A, Kaiser SP, et al. 2007. Aortic valve replacement in octogenarians: risk factors for early and late mortality. *Ann Thorac Surg* 83:1651-6.
- Rahimtoola SH. 2003. Choice of prosthetic heart valve for adult patients. *J Am Coll Cardiol* 41:893-904.
- Potter DD, Sundt TM 3rd, Zehr KJ, et al. 2005 Operative risk of reoperative aortic valve replacement. *J Thorac Cardiovasc Surg* 129:94-103.
- Ruel M, Chan V, Bédard P, et al. 2007. Very long-term survival implications of heart valve replacement with tissue versus mechanical prostheses in adults <60 years of age. *Circulation* 116(11 Suppl):1294-300.
- Svennevig JL, Abdelnoor M, Nitter-Hauge S. 2007. Twenty-five-year experience with the Medtronic-Hall valve prosthesis in the aortic position: a follow-up cohort study of 816 consecutive patients. *Circulation*. 116:1795-800.
- Vogt PR, Brunner-LaRocca H, Sidler P, et al. 2000. Reoperative surgery for degenerated aortic bioprostheses: predictors for emergency surgery and reoperative mortality. *Eur J Cardiothorac Surg* 17:134-9.