

Outcome after Aortic Valve Replacement: Comparison of Homografts with Mechanical Prostheses

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Background and aim of the study: Aortic valve replacement (AVR) in younger patients is conventionally performed using a mechanical prosthesis (MP), although homograft (HG) implantation is an accepted alternative. This study compares, retrospectively, the follow up of these two dissimilar prostheses.

Methods: Since 1990, a total of 147 Sorin Bicarbon[®] MPs and 285 HGs have been implanted at the authors' institution, and compared statistically for survival, reoperation rate and valve-dependent complications. Only patients aged <70 years were included in the study.

Results: The demographic parameters of both patient groups differed with regards to gender, age at the time of implantation, and duration of follow up. Survival was superior in the HG group (log-rank, $p = 0.01$). Sixteen of 42 late deaths in the MP group were valve-related due to cerebral infarction ($n = 7$), ventricular arrhythmias ($n = 3$), or ventricular failure ($n = 6$). Six of 24 deaths after HG implantation were valve-related (all prosthesis infections). The choice of valve type and patient age were independent risk

factors in the multivariate analysis. Freedom from reoperation was superior after MP implantation (log rank, $p = 0.007$); in six MP patients the indications for redo surgery were prosthesis infection ($n = 2$) and paravalvular leak ($n = 4$). In 20 HG patients, redo surgery was required due to prosthesis infection ($n = 12$), stenotic degeneration ($n = 2$), regurgitation > grade II ($n = 4$), or paravalvular leak ($n = 2$). Age at the time of implantation and valve type were independent risk factors. Thromboembolic complications were mainly seen in MP patients (log rank, $p < 0.001$): there were five ischemic infarctions and 11 transient ischemic attacks (TIAs) compared to three TIAs among HG patients. Cerebral bleeding was found in only 18 cases after MP implantation, and in no cases after HG implantation. In the multivariate analysis, the type of prosthesis was an independent risk factor. **Conclusion:** As expected, these data confirm a longer time period without need for reoperation after MP implantation, but demonstrate a significantly higher survival and fewer complications after AVR with HG.

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The use of homografts (HGs) in aortic valve replacement (AVR) is a common alternative to mechanical or biological valve prostheses, as there is no need for anti-coagulation and near-physiological hemodynamic conditions can be achieved. Especially in young patients, there is no satisfactory therapeutic solution for all situations; consequently, the indication for anti-coagulation with mechanical prostheses (MPs) on the

one hand, and the limited durability of biological prostheses on the other hand, requires that an individual decision be made for each patient.

Among biological prostheses, HGs were first used for aortic valve replacement in 1962 (1,2), and have since been employed routinely in some cardiac surgical departments since the early 1970s. At the authors' institution, HGs have been implanted frequently since 1992 and have provided good mid-term results (4) comparable with those reported by O'Brien (3), which related to the world's largest patient sample, and to stented biological prostheses (5).

The study aim was to evaluate outcome after AVR in younger patients and to compare the results obtained with HGs and MPs.

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Table I: Patient demographics and follow up data.

Parameter	Homografts (n = 285)	Mechanical prostheses (n = 147)	p-value
Period of implantation	1992-2004	1990-1998	
Age at implantation (years)*	50.0 (19.6-70.0)	54.8 (19.7-70.0)	0.01
Gender ratio (F:M)	75:210	22:125	0.02
Follow up (months)*	64.3	97.5	<0.001

*Values are mean (range).

Clinical material and methods

Patient demographics

The age cut-off at the time of surgery was 70 years for both patient groups. The main indication for AVR was stenosis, followed by regurgitation and combined diseases. Those patients with acute valve-affecting endocarditis, and those who received replacements for pre-existing prostheses were entered into a further analysis (see Tables I and II).

In order to compare the two groups, differences were evaluated in terms of survival after surgery, the need for reoperation, and valve-related events. All results and follow up data were reported in accordance with the recommendations of the Ad Hoc Liaison Committee in Guidelines for Reporting Morbidity and Mortality after Cardiac Valvular Operations (7).

Homografts

Between May 1992 and June 2004, a total of 354 patients underwent valve replacement with aortic HGs at the authors' institution, and currently constitute a prospective annual follow up. The grafts were harvested from cardiac transplant recipients, treated with an antibiotic cocktail containing amikacin, ciprofloxacin, vancomycin, amphotericin B and metronidazole, and subsequently stored in a homograft bank at -197°C using dimethyl sulfoxide in liquid nitrogen [6]. No attempt was made to match blood groups or HLA antigenic status. The grafts were implanted using either the subcoronary (n = 75) or root replacement (n = 279) technique.

Ultimately, a total of 285 patients was included in the study. Because of the complex cardiac changes involved, children with congenital heart disease (n = 32) were excluded, as well as older patients aged >70 years (n = 26) and those who had undergone additional mitral valve surgery (n = 11).

Mechanical prostheses

Patients who received a Sorin Bicarbon valve were selected as being representative for all models of mechanical bileaflet prostheses implanted. The Sorin

Bicarbon was launched in 1990, and between 1990 and 1998 a total of 147 patients underwent AVR at the authors' institution during a prospective, multicenter trial. The target International Normalized Ratio (INR) range for postoperative anticoagulation was 2.5 to 3.

Statistical analysis

All recorded data were compared statistically using *t*-tests and chi-square tests. A multivariate analysis for all patients was performed to identify independent factors which influenced mortality. Survival rate, freedom from redo surgery and absence of valve-related events were calculated as cumulative events according to Kaplan-Meier and the log rank test with documentation of the patients at risk. All p-values were two-tailed; results were considered to be statistically significant if the p-value was ≤0.05. The software package SPSS 14.0 for Windows was used to calculate these data.

Table II: Indications for surgery.

Indication	Homografts (n = 285)	Mechanical prostheses (n = 147)
Valve stenosis	108 (38)	38 (34)
Valve regurgitation	89 (31)	47 (31)
Combined valve diseases	47 (17)	16 (14)
Acute valve endocarditis	32 (11)	26 (14)
Replacement of pre-existing valve prosthesis	9 (3)	20 (7)
Co-procedures		
Coronary bypass	24 (8)	11 (7)
Mitral valve repair	-	-
Replacement of ascending aorta	36 (13)	13 (9)

Values in parentheses are percentages.

Results

Patient characteristics

In total, 432 patients were allocated to the MP (n = 147) and HG (n = 285) groups. The two groups were seen to be significantly different in terms of age at the time of implantation and during the follow up period, and also in gender (see Table I).

Survival

All-cause mortality within 30 days after surgery was 5.0% among HG patients, and 4.1% among MP patients (p = NS). During the long-term follow up, survival among HG patients became superior to that of MP patients. Typically, postoperative survival after 10 years was 84.4% for HG patients, and 65.9% for MP patients (p = 0.012) (Fig. 1). In the multivariate analysis, gender could be excluded as a risk factor for adverse outcome in this patient cohort. Both, age at the time of implantation (p = 0.001) and type of valve prosthesis (p = 0.043), were identified as independent risk factors for decreased survival.

Among 24 late deaths in the HG group, six (2.0%) were valve-related, and all of these patients died as a result of prosthesis infections. Among the MP patients, 42 died during the follow up, and 16 of these deaths (10.9%) were valve-related. None of these prosthesis infections proved fatal; rather, deaths were due to congestive heart failure, ventricular arrhythmias and stroke (Table III).

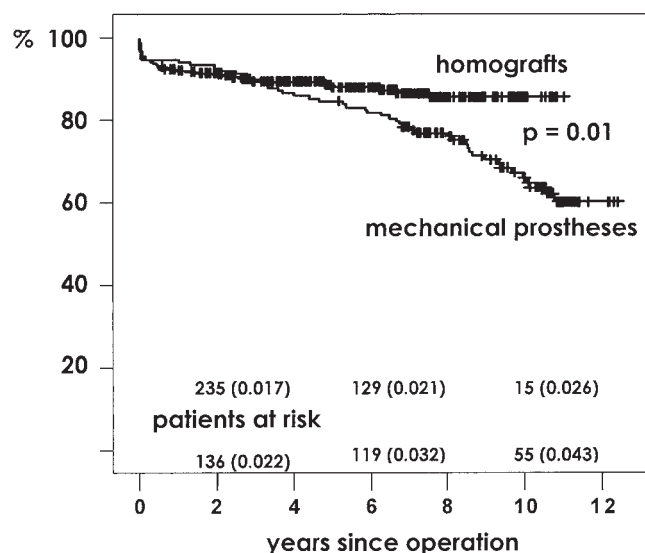


Figure 1: Survival curves (Kaplan-Meier) after aortic valve replacement with homografts or with mechanical prostheses, including early mortality. Numbers of patients at risk are displayed at 2, 6 and 10 years postoperatively; values in parentheses are standard errors and 95% confidence limits for all figures (log-rank test).

Table III: Causes of death after aortic valve replacement with homografts versus mechanical prostheses.

Cause of death	Homografts (n = 285)	Mechanical prostheses (n = 147)
Congestive heart failure	-	6 (4.1)
Ventricular arrhythmia	-	3 (2.0)
Stroke	-	7 (4.8)
Prosthesis infection	6 (2.1)	-
All causes	6 (2.1)	16 (10.9)

Values in parentheses are percentages

Freedom from reoperation

Freedom from reoperation after 10 years was 86.5% for HG patients and 96.4% for MP patients (p = 0.007) (Fig. 2). Among 147 patients who received MPs, only six required redo surgery due to paravalvular leak and prosthesis infection. In the HG group, 20 of 285 patients had graft replacements: in this group, in addition to infection and leakage, the reasons for homograft explantation were degenerative alterations such as graft stenosis and regurgitation of grade II or more (Table IV). Multivariate analysis showed age at the time of implantation (p = 0.04) and the type of valve prosthesis (p = 0.01) to be risk factors for a need for redo surgery, but no correlation was identified between gender and reoperation.

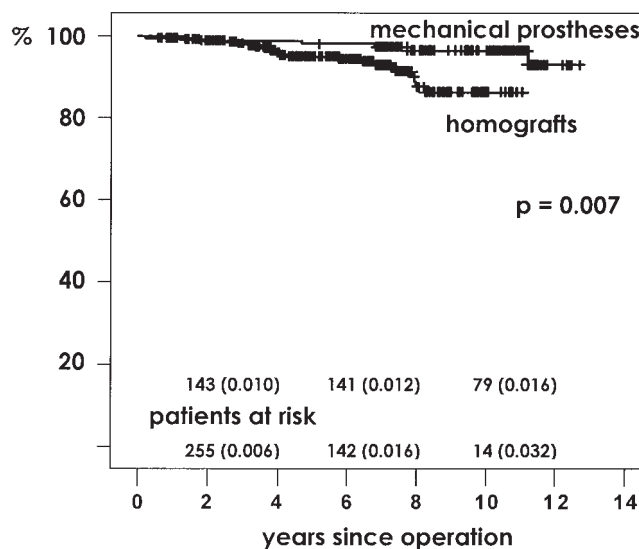


Figure 2: Freedom from redo surgery for both patient groups after aortic valve replacement. Fewer redo operations were necessary in the mechanical prosthesis group.

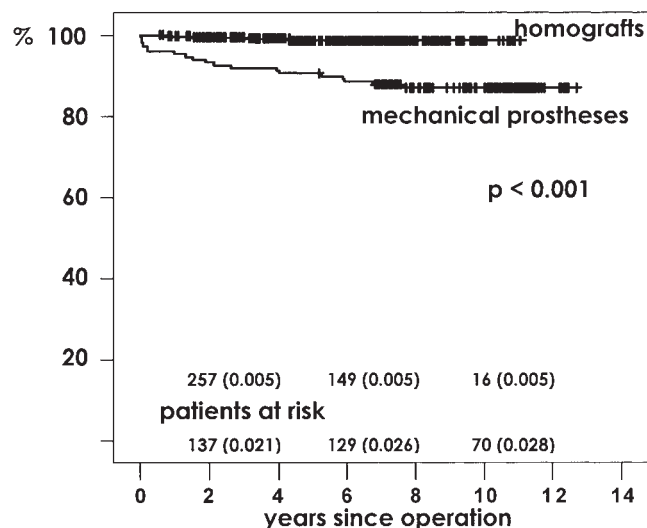


Figure 3: Comparison of freedom from valve-related events. Events were defined as bleeding or thromboembolic complications after valve replacement, not leading to redo surgery or death. The event rate was higher in the mechanical prosthesis group.

Valve-related complications

Complications associated with AVR which did not lead to explantation of the grafts or prostheses were registered as ischemic or hemorrhagic cerebral events (Fig. 3). The need for anticoagulation in MPs and the possibility of dosage mistakes was reflected in a significantly higher rate of complications here ($p < 0.001$). Transitory ischemic attack (TIA) occurred in only three HG patients (1.1%), but in 34 patients with MPs (23.1%). Ischemic and hemorrhagic strokes were also identified in addition to TIAs (Table V). Multivariate analysis identified the type of valve prosthesis as a significant risk factor for valve-related complications ($p < 0.001$), whereas neither age nor gender predicted any risk for valve-related complications among the study cohort.

Table IV: Freedom from reoperation after aortic valve replacement with homografts versus mechanical prostheses.

Cause of reoperation	Homografts (n = 285)	Mechanical prostheses (n = 147)
Prosthesis infection	12 (4.2)	2 (1.4)
Stenotic degeneration	2 (0.7)	-
Regurgitation > grade II	4 (1.4)	-
Paravalvular leak	2 (0.7)	4 (2.7)
All causes	20 (7.0)	6 (4.1)

Values in parentheses are percentages.

Discussion

The results obtained showed that the type of valve replacement was indeed a risk factor for adverse outcome, with mechanical prostheses shown as an independent risk factor for valve-related complications and mortality, whereas homograft implantation was associated with a greater risk for redo surgery.

The aim of implanting HGs for AVR at the authors' institution was to obtain near-normal hemodynamic conditions, which should be superior to those achieved with stented xenografts, with comparable risk for mortality, function, and durability, as reported previously (4). It might also be expected that the durability of MPs would be higher (at least than biological prostheses), because of their different construction and the use of materials which are not susceptible to degeneration. Sorin, as the manufacturer of the Bicarbon prosthesis, have reported details of the implantation of more than 165,000 valves within 15 years, as stated by Borman and De Riberolles (8), without any structural failure ($n = 2078$). On the other hand, the mandatory need for anticoagulation in this group is also known to be a risk factor for complications (9).

Especially in patients aged <60 years, the choice of an aortic valve substitute is difficult because of the limited durability of xenografts on one hand, and the hemodynamic performance and need for anticoagulation with MPs on the other hand, as mentioned above. In contrast to valve prostheses, HGs function with near-normal hemodynamics and therefore are predestined for people with an active lifestyle who also wish to avoid prolonged anticoagulant therapy. If these persons accept a higher risk after redo surgery than might be expected with xenoprosthesis, then the implantation of a HG is recommended at the authors' department (10).

Although the two present patient groups differed demographically, only "hard" statistical criteria were chosen in order to achieve a reliable comparison of

Table V: Absence of (non-lethal) valve-related events.

Cause	Homografts (n = 285)	Mechanical prostheses (n = 147)
TIA	3 (1.1)	11 (7.5)
Ischemic stroke	-	5 (3.4)
Hemorrhagic stroke	-	18 (12.2)
All causes	3 (1.1)	34 (23.1)

Values in parentheses are percentages.
TIA: Transitory ischemic attack.

these unequal alternatives for AVR. As reported by Myken et al. (11), who compared mechanical with stented porcine prostheses, survival among the present patients was computed after surgery, freedom from reoperation, and valve-related events. According to these results, an inferior actuarial survival was identified in patients with MPs, this being due to the increased coagulation-related complications in this subgroup (Fig. 1). The same finding was noted by Khan et al. (12), who also compared bioprostheses with mechanical valves and showed that, due to anticoagulation therapy, patients with mechanical valves had an increased risk of bleeding and embolic events. In the present series this also led to a significant decrease in survival (Table III). Additional reasons identified for valve-related deaths for MPs were ventricular failure and arrhythmias, as described by others [9]. However, these were not seen in the HG group and may have been associated with the better hemodynamic function here [4].

The rate of redo surgery was expected to be higher in patients with HGs, and this proved correct (Fig. 2). When comparing the present HG group with results obtained with other patients following implantation of the Sorin Bicarbon valve, Borman and De Riberolles (8) showed a higher independence of redo surgery of 98.2% in a 10-year multicenter follow up (in the present study alone it was 93.3%) which at least was statistically significantly different to the present HG patients ($p < 0.001$, log rank test).

The indications for HG explantation included, as well as the expected degeneration, a high rate of graft infections (Table IV), which could not be associated with pre-existing endocarditis and contrasted with the results of Lund et al. (13), who reported fewer cases with infections related to degeneration. In the present study, only one patient with streptococcal endocarditis developed an infectious relapse three months after HG implantation and died during the early phase after redo surgery due to multi-organ failure (14). All other cases were registered for 1,000 days after surgery (or later), and therefore could not be associated with the implantation or the graft preparation. Although no specific explanation was provided for the HG infections, the reasons have been postulated as a possible lower resistance against bacterial infectious agents in cryopreserved HGs, than in glutaraldehyde-fixed biological prostheses.

Nonetheless, graft infections and degenerative changes of the homografts on the one hand, and interference with the coagulatory system with MPs on the other hand, seemed to be the main problems for survival and reoperation rate. Other non-lethal, valve-related problems were also seen in correlation to the need for anticoagulation in the MP group. At the

authors' institution, patients receiving HG implantation are not administered anticoagulation or platelet aggregation inhibitors at any time after surgery, and in only five cases showed TIAs, whereas significantly more ischemic events occurred in the mechanical valve group. In addition to TIAs, there were also hemorrhagic and ischemic cerebral infarctions (Table V), which makes the use of MPs less safe than might be expected, and often underestimated. However, the results obtained for the Sorin Bicarbon prostheses were comparable to those obtained with other, more commonly used mechanical valve substitutes (15).

In conclusion, the data obtained in the present study demonstrated superior survival and freedom from valve-related complications after AVR with HGs, while those patients who received MPs had a favorable freedom from redo surgery. It is remarkable that the need for anticoagulation as a mandatory requirement after mechanical valve replacement contributed most to mortality and valve-related complications. The most common cause for a higher frequency of redo surgery among HG patients was, besides degenerative alterations, a higher rate of graft infection.

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