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Pulmonary Homografts for Aortic Valve Replacement: Long-term Comparison with Aortic Grafts

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ABSTRACT

Objective: The use of homografts for aortic valve replacement (AVR) is an alternative to mechanical or biological valve prostheses, especially in younger patients. This retrospective comparative study evaluated our single-center long-term results, with a focus on the different origins of the homografts.

Methods: Since 1992, 366 adult patients have undergone AVR with homografts at our center. We compared 320 homografts of aortic origin and 46 homografts of pulmonary origin. The grafts were implanted via either a subcoronary technique or the root replacement technique. We performed a multivariate analysis to identify independent factors that influence survival. Freedom from reintervention and survival rates were calculated as cumulative events according to the Kaplan-Meier method, and differences were tested with the log-rank test.

Results: Overall mortality within 1 year was 6.5% (21/320) in the aortic graft group and 17.4% (8/46) in the pulmonary graft group. In the pulmonary graft group, 4 patients died from valve-related complications, 1 patient died after additional heterotopic heart transplantation, and 1 patient who entered with a primary higher risk died from a prosthesis infection. Two patients died from non–valve-related causes. During the long-term follow-up, the 15-year survival rate was 79.9% for patients in the aortic graft group and 68.7% for patients in the pulmonary graft group ($P = .049$). The rate of freedom from reoperation was 77.7% in the aortic graft group and 57.4% in the pulmonary graft group ($P < .001$). The reasons for homograft explantation were graft infections (aortic graft group, 5.0%; pulmonary graft group, 6.5%) and degeneration (aortic graft group, 7.5%; pulmonary graft group, 32.6%).

Conclusion: Our study demonstrated superior rates of survival and freedom from reintervention after AVR with aortic homografts. Implantation with a pulmonary graft was associated with a higher risk of redo surgery, owing to earlier degenerative alterations.

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INTRODUCTION

The use of homografts for aortic valve replacement (AVR) is a good alternative to mechanical or biological prostheses, because anticoagulation medication can be avoided and excellent hemodynamic conditions can be achieved.

After the introduction of homografts for AVR in 1962 [Ross 1962; Barratt-Boyes 1969], the early preparation and preservation techniques generated fewer favorable long-term results until the establishment of antibiotic sterilization [Yacoub 1970] and cryopreservation techniques [Hehrlein 1971; O'Brien 1987; Schütz 1993; Fischlein 1995; Mirabet 2008]. After publications [Barratt-Boyes 1969; Mirabet 2008] that promised good midterm results after homograft implantation, a program based on our in-house homograft bank was launched in our institution. Because of the growing demand for homografts, the use of homografts of pulmonary origin was also established; however, early degeneration of homografts may lead to hemodynamic compromise. In this retrospective study, the outcomes after homograft implantation were evaluated with respect to the origin of the grafts, with special attention paid to infections and early degeneration.

MATERIALS AND METHODS

Homografts

The homografts were harvested from the hearts of cardiac transplant recipients. After treatment with an antibiotic cocktail containing amikacin, ciprofloxacin, vancomycin, amphotericin B, and metronidazole, the homografts were stored in liquid nitrogen at –197°C in our in-house homograft bank, with dimethyl sulfoxide used as a cryoprotectant [Schütz 1993]. Overall, 320 aortic homografts and 46 pulmonary homografts were implanted.

Surgical Techniques

Between 1992 and 1995, homografts (n = 75) were implanted via a subcoronary technique that conserved the patient's aortic root. All other implantations occurred via root replacement, which requires reimplantation of the coronary arteries (n = 291) (Figure 1). All procedures were performed via a median sternotomy and with cardiopulmonary bypass. The septal temperature depended on the need for additional cardiac arrest and ranged between 16.0°C and 32.0°C (mean, 26.6°C) in both the pulmonary graft and aortic graft groups. The mean (±SD) bypass time was 170 ± 52 minutes in the aortic graft group

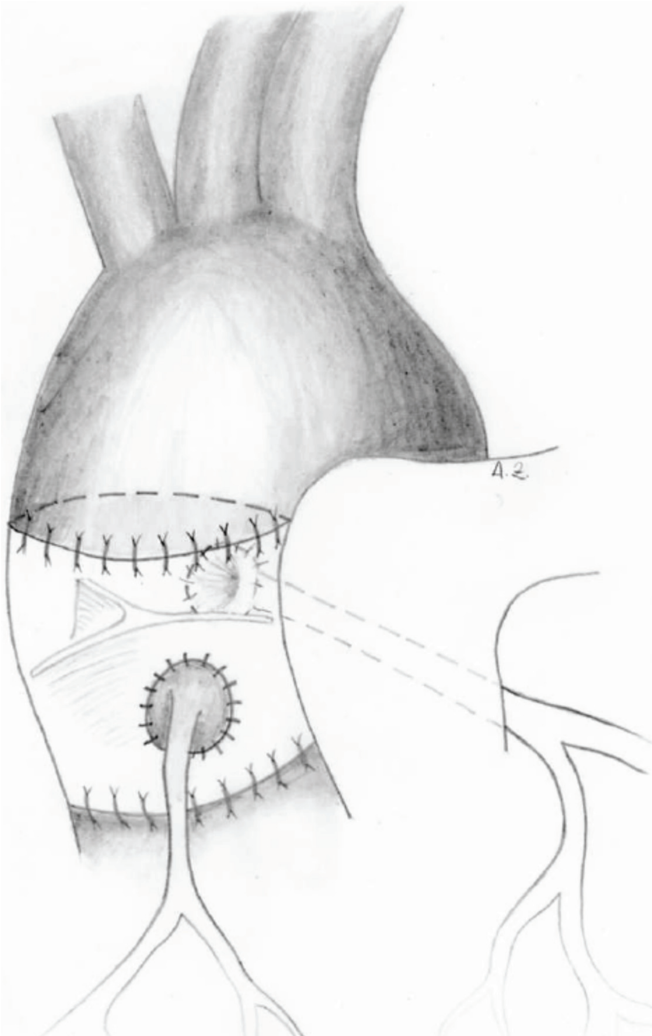

Figure 1. The homograft is implanted into the desired position.

and 163 ± 49 minutes in the pulmonary graft group (difference not statistically significant). The mean aortic-clamping time was 121 ± 30 minutes in the aortic graft group and 126 ± 30 minutes in the pulmonary graft group (not significantly different). Standard cardioplegic arrest was performed with Bretschneider solution (HTK; Dr. Franz Köhler Chemie, Bensheim, Germany). In 48 aortic graft cases and 6 pulmonary graft cases, Buckberg blood cardioplegia was used.

Study Design

Starting in May 1992, 432 patients underwent AVR with homografts at our institution. Patients with congenital heart diseases (n = 55) were not included in this study. The patients participated in annual prospective follow-ups that included echocardiography, electrocardiography, and history-taking evaluations, which were completed for 97% (366) of the patients. The institutional review board provided dispensation for this retrospective study.

Echocardiographic Analysis/Follow-up according to the Origin of the Graft

To compare the long-term hemodynamic results of aortic grafts and pulmonary grafts, we assessed the following parameters by echocardiography: end-diastolic diameter (in millimeters), left ventricular ejection fraction, peak pressure gradient via the homograft (in millimeters of mercury), regurgitation grade (0-III), and root diameter (in millimeters).

All of these data provide information about overall graft function. Structural alterations to grafts were described according to Yacoub et al [1995]. Regurgitation was graded as absent (grade 0), mild (grade I), moderate (grade II), or severe (grade III). Stenosis was defined as moderate at a mean pressure gradient between 30 and 50 mm Hg and as severe at a mean pressure gradient >50 mm Hg. In addition, we analyzed the effects of the type of graft (aortic versus pulmonary), the implantation technique (subcoronary versus root replacement; Figure 1), and patient sex. Postoperatively, patients underwent thorough echocardiographic reexaminations and reinterview evaluations once a year in our outpatient department.

Data Acquisition and Analysis

Surgical results and follow-up data were reported in accordance with the recommendations of the Ad Hoc Liaison Committee [Edmunds 1996]. All recorded data were examined statistically via analysis of variance, the Student t test, the chi-square test, and the Wilcoxon test as appropriate for the comparison of means. A *P* value <.05 was considered statistically significant.

Survival and freedom from reoperation were analyzed as cumulative events according to the Kaplan-Meier method and were evaluated statistically with the log-rank test, with documentation of the patients at risk. Statistical analyses were carried out with SPSS (version 17.0. for Windows; SPSS, Chicago, IL, USA).

RESULTS

Demographics

Of 366 adult patients, 253 (72.0%) were male. The mean age at homograft implantation was 51.6 years (range, 12-84 years), with a mean (±SD) follow-up time of 9.4 ± 3.8 years (maximum, 16.2 years). The indications for AVR with either an aortic graft or a pulmonary graft are shown in Table 1. Additional surgical procedures (stand alone or in combination) were necessary in 55 patients for replacement of the ascending aorta, 12 mitral valve operations, 1 tricuspid valve reconstruction, and 39 coronary artery bypass grafts.

Echocardiographic Results

The left ventricular ejection fraction increased slightly but not significantly in both groups after surgery, and the left ventricular end-diastolic diameter decreased in both groups. In the aortic graft group, the postoperative root diameter showed a progression from a mean diameter of 28 mm to 33 mm after 15 years. The peak pressure gradient increased from 10.5 mm Hg to 37 mm Hg after 15 years, and aortic valve regurgitation increased from less than grade I after

Table 1. Indication for Surgery

Indication for Surgery	Patients, n	Aortic Grafts, n	Pulmonary Grafts, n	*P*
Degenerative	298	259	39	NS*
Infectious	51	46	5	NS
Aortic valve stenosis	98	94	4	NS
Aortic valve regurgitation	65	47	18	NS
Combined aortic valve diseases	59	47	12	NS
Replacement of preexisting prostheses	8	8	0	NS

*NS indicates not statistically significant.

surgery to grade II to III after 15 years without significant differences between the aortic graft and pulmonary graft groups. The echocardiographic results are summarized in Table 2.

Bleeding and Thromboembolism

Because anticoagulation therapy is not required after homograft implantation, some patients received acetylsalicylic acid or coumarin therapy for other reasons, such as coronary artery disease or atrial fibrillation. In the early postoperative course, major bleeding was found in 16 aortic graft cases and 2 pulmonary graft cases. A hemodynamically relevant tamponade occurred in 6 aortic graft cases and 2 pulmonary graft cases. No cerebral bleeding occurred. Two patients in the aortic graft group presented with single episodes of upper gastrointestinal bleeding, and 3 patients in the aortic graft group experienced epistaxis. Only 1 patient in the pulmonary graft group with coumarin therapy experienced epistaxis. Exclusively in the pulmonary graft group, 2 strokes and 11 transitory ischemic attacks were registered during the observation period.

Survival

The 30-day mortality rate was 3.7% (10/320) in the aortic graft group and 15.2% (7/46) in the pulmonary graft group. Two patients in the pulmonary graft group died from endocarditis after prosthesis infection. One patient who underwent additional heterotopic heart transplantation died, and 2 other patients died from non–valve-related causes. The mortality rate within 1 year was 6.5% in the aortic graft group (21/320) and 17.4% in the pulmonary graft group (8/46) (P = .43, nonsignificant). The survival rate after 5 years was 89.6% in the aortic graft group and 76.0% in the pulmonary graft group (P = .001). After 10 years, the survival rate was 85.6% in the aortic graft group and 76.0% in the pulmonary graft group (P = .024). During the long-term follow-up (Figure 1), the 15-year survival rate was 79.9% among patients with homografts of aortic origin and 68.7% among patients with homografts of pulmonary origin (P = .049).

Freedom from Reintervention

The rate of freedom from reintervention after 1 year was 99.1% in the aortic graft group and 97.8% in the pulmonary graft group (P = .08). At 5 years after surgery, the rates were 95.8% and 82.4%, respectively (P = .001). After 10 years, 84.5% of the patients in the aortic graft group and 64.0% of the patients in the pulmonary graft group were free from reintervention (P < .001). The long-term freedom of reintervention (after 15 years) was 77.7% in the aortic graft group and 57.4% in the pulmonary graft group (P < .001; Figure 2).

The main reason for homograft replacement was graft infection. Infections necessitated redo AVR in 16 patients in the aortic graft group and 3 patients in the pulmonary graft group (difference not statistically significant). Degeneration was more often seen in the pulmonary graft group (15 patients) than in the aortic graft group (24 patients). In contrast to the aortic graft group, regurgitation was the main cause of degenerative alteration in the pulmonary graft group and led to graft explantation. Of these patients, 53 underwent classic redo surgery with mechanical or xenobiotic prostheses. Two patients specifically asked for another homograft, and 3 patients underwent minimally invasive transapical valve implantation.

Table 2. Echocardiography Data*

Parameter	Postoperative	Follow-up 5 Years	10 Years	15 Years
Root diameter, mm				
AG	28.3	30.7	29	33
PG	30.0	30.5	29	—
Peak pressure gradient, mm Hg				
AG	10.5	15.5	20.6	37
PG	11.2	9.8	11.0	—
Aortic valve regurgitation, grade (0-III)				
AG	0.43	0.99	0.91	2.5
PG	0.96	1.15	1	—

*AG indicates aortic graft; PG, pulmonary graft.

DISCUSSION

The intention to use homografts for AVR in our department was to obtain excellent hemodynamic conditions that were superior to those for stented xenografts and to obtain improved long-term durability, following the publication of promising studies that described enhanced preservation methods [O'Brien 1987; Mirabet 2008]. Because of an overall lack of grafts, pulmonary grafts were also used in the aortic position.

The results we have presented focus on the implantation of pulmonary grafts versus aortic grafts for AVR and their long-term follow-up results. As suspected, we can now accept our hypothesis that the need for redo AVR (Figure 3) and even survival rates (Figure 2) are significantly worse for patients who received pulmonary grafts than for those who received aortic grafts. The survival results for the

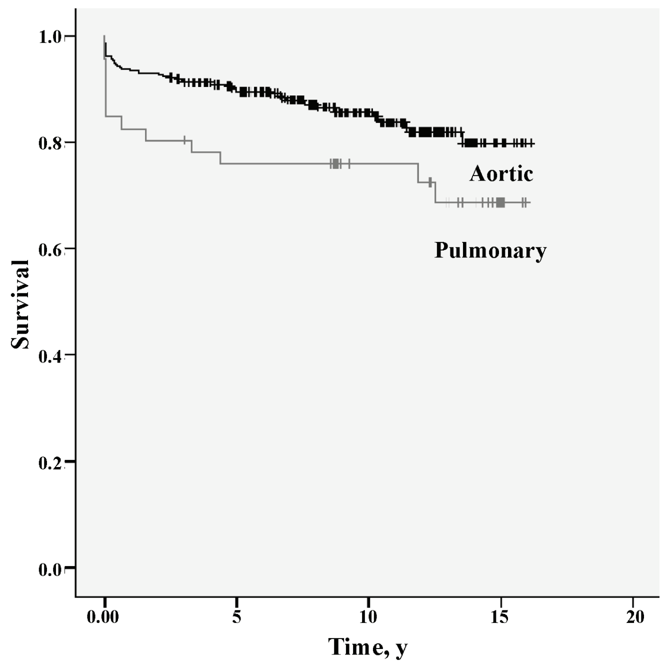

Figure 2. Long-term follow-up of survival among patients with homografts of aortic and pulmonary origin.

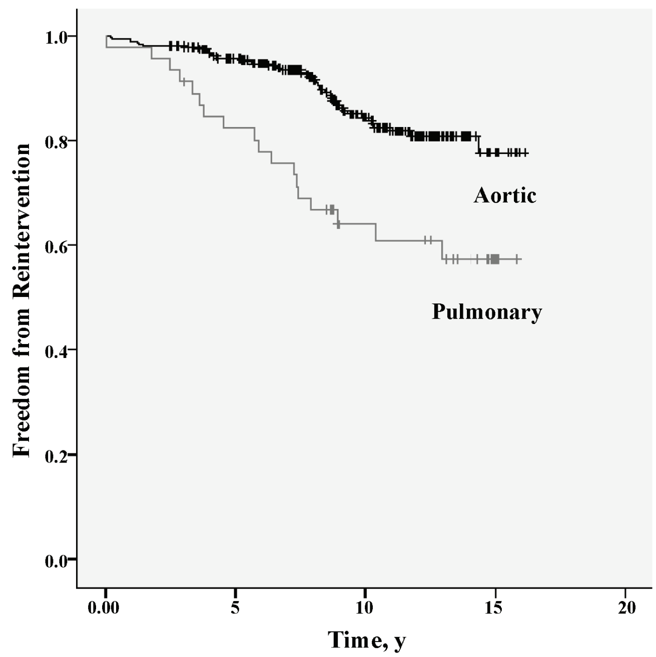

Figure 3. Long-term follow-up of freedom from reintervention among patients with homografts of aortic and pulmonary origin.

aortic group are comparable to results reported by other investigators regarding homograft implantation [Lund 1999; O'Brien 2001; Kilian 2004; Mirabet 2009] or after AVR with xenografts [Frater 1998; Borger 2006]. In contrast to early publications regarding the use of pulmonary grafts for AVR [Gorczynski 1982; Mair 1995; Yacoub 1995], the incidence of graft failure in our series of patients was higher in patients who received pulmonary grafts. The higher early mortality in patients who received pulmonary grafts was the most obvious difference between the 2 graft groups. Because of this fact, we cancelled the implantation of pulmonary grafts at our institution; however, mortality at 1 year after implantation of a homograft was independent of the anatomic origin of the graft. A possible explanation for this early-mortality result is that early degeneration of pulmonary valve homografts might occur mostly in the first year after implantation.

The necessity for graft explantation is reflected in the freedom from redo AVR, which is another major issue of interest in comparing aortic and pulmonary grafts. The rate of freedom from redo AVR after 15 years was 77.7% for an aortic graft and 57.4% for a pulmonary graft in the aortic position ($P < .001$; Figure 3). The 2 graft groups showed no significant differences in the reasons for graft explantation. This finding may be biased by the smaller number of pulmonary grafts. A remarkable finding was the higher number of degenerative alterations, especially in the rate of regurgitation, that led to pulmonary graft explantation. Our echocardiographic data revealed increases in the regurgitation rate and the pressure gradient in both groups, but the differences were not statistically significant.

In a comparison of AVR using homografts with the Ross operation, Hörer [2009] showed that the origin of the graft indeed influenced the outcome and follow-up of the subsequently performed surgery. Owing to the positive results for pulmonary autografts in the aortic position as performed in the Ross operation, this transpositioning procedure was replicated with cryopreserved grafts. This conservation and storing process might have affected pulmonary grafts more negatively than aortic grafts. This hypothesis might explain why the major problem in the Ross procedure is not the pulmonary autograft in the aortic position but the degenerated or, more likely, calcified homograft in the pulmonary position. Some morphologic studies have shown cusp tissue degeneration with tears and calcification, as well as pannus growth on the flow and nonflow surfaces of the cusps, when pulmonary grafts are implanted in the pulmonary position [Luk 2007]. A significant loss of cuspal tissue on one side was described in that report, but there was no evidence of inflammation. Few reports have discussed long-term morphologic changes in explanted pulmonary homografts after the Ross procedure [Tweddell 2000; Butany 2004]. Such changes have been described as a significant loss of cuspal tissue, as well as calcification and ossification at the basis of the cusps. Such changes contribute to stenosis, incompetence, and eventual failure that necessitate surgical explantation.

Although some authors have described the process of cryopreservation and its potential side effects as such, no explicit examination has yet been performed with respect to the origin of the valve. The results obtained at our institution suggest a difference in outcomes that is related to the origin of the graft. In contrast to early publications regarding the use of pulmonary grafts for AVR [Gorczynski 1982; Mair 1995; Yacoub 1995], the incidence of graft failure was higher in patients who received pulmonary grafts than in those who received aortic grafts, an observation that led to the decision to cease implantation of pulmonary grafts in the aortic position at our institution. The actual number of degenerations was higher than expected, especially in the pulmonary graft group. In contrast, as previously described [Riberi 1997; Niwaya 1999; Naegele 2000], homografts are especially used in our institution for difficult cases involving patients presenting with native aortic valve endocarditis, including root abscesses [Gulbins 2002].

CONCLUSION

AVR using homografts has been performed at our institution for 16 years. Our experience has shown that the use of a pulmonary graft leads to worse results after AVR; we therefore cancelled the implantation of homografts of pulmonary origin. The data we have presented confirm both a higher rate of graft explantation and increased mortality in patients who receive a pulmonary graft. Our data for survival and freedom from redo procedures for aortic grafts are comparable to the data of others who have described similar techniques or AVR procedures involving xenoprostheses.

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