Are pulmonary homografts which were subjected to pulmonary hypertension more appropriate for aortic valve replacement than normal pulmonary homografts? A long-term multicentric echography study

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Abstract

Objective: To compare long-term results of the European Homograft Bank (LHB) cryopreserved pulmonary homograft in left ventricular outflow tract (LVOT) subjected to pulmonary hypertension with those subjected to normal pulmonary pressure. The mid-term study of this material published in 1997 showed different results. Methods: Ninety EHB cryopreserved PHG were used for LVOT reconstruction in different European centres between May 1989 and December 1995. PHGs were classified in two groups: (1) Pulmonary hypertension PHG (procured from recipients of heart/heart-long transplantation) and (2) Normal pulmonary pressure PHG (procured from multiorgan donors and cadavers). Significant echocardiography changes were defined as a stenosis with gradient of more than 30 mmHg and/or insufficiency of > 2 + . Statistical analysis is calculated by the Kaplan–Meier survival curves, while differences in prevalence by the Log-Rank test. Results: Follow-up (FU) was available in 69 cases (76.7%): 46 in group 1 and 23 in group 2. Five patients have been excluded from the study because of early homograft explantation (technical problems or early valve incompetence). Fourteen out of 43 cases of group 1 (32.6%) and seven out of 21 cases of group 2 (33.3%) have been explanted after 2.5–88 months and 7–88 months, respectively. Significant echography changes have been found in 19 of 43 (44.18%) of group 1 and 11 of 21 cases (52.38%) of group 2 during the follow-up. Histology showed essentially wear and tear induced lesions. Mean FU was 36.9 (range, 6–88) and 41.3 months (range, 4–88) for group 1 and 2, respectively. No significant difference in the long-term outcome have been found between the two groups (P = 0.38). Conclusion: Contrary to our previous echocardiography study of mid-term implants the long-term follow up of the PHGs implanted in the LVOT did not show better function of the pulmonary homografts subjected to pulmonary hypertension than those with normal pulmonary pressure. The high failure rate of the PHGs should discourage their use for LVOT reconstruction. Further echocardiography studies of remaining PHGs implanted in the LVOT, and gross and microscopic explant studies are required to judge on the definitive outcome of these grafts. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Pulmonary homograft; Aortic valve replacement; Echocardiography

1. Introduction

Considering the excellent long-term results with the pulmonary autograft used for reconstruction of the left ventricular outflow tract [1,2] and according to the investigations of Gorczynski [3] and Gerosa [4], which proved that the PHG can withstand higher mechanical stress in systemic circulation, many cardiac surgeons have used the pulmonary homograft, rather than autograft, for reconstruction of the left ventricular outflow tract (LVOT). The latest considering the invasivity of the Ross procedure. However, use of a cryopreserved pulmonary homograft for this purpose has many controversies and is at the present time almost completely abandoned for elective cases [4,5]. During the early 1990s this method was rather popular and many European Heart Surgery centres have reported implantation of this EHB graft in several cases [4–10].

During the procurement of the human heart valves, one have observed macroscopic differences between the
pulmonary homografts, related to pulmonary hypertension and those with normal pulmonary pressure [7] which correspond with the earlier publications of Davies [11] and Wagenvoort [12]. This was one of the reasons which encouraged us to study the clinical course and compare these two groups of the PHGs.

Earlier we have published mid-term results of the multicentric echography study of the 52 pulmonary homografts used for LVOT reconstruction, comparing the PHGs related to pulmonary hypertension with those related to normal pulmonary pressure [7]. The aim of this study was to compare the long-term echography outcome of these two groups of cryopreserved homografts. The mid-term results of a comparable group published by the same institution in 1997 have shown a different results.

2. Materials and methods

2.1. Pulmonary homografts and patient data

A total of 90 EHB cryopreserved PHGs have been implanted in the LVOT in different European Cardiac Surgery centres between May 1989 and December 1995. The recipient age varied from 7 days to 80 years (mean age 41.5 years). Sixty-three patients were male and 27 female (ratio 2.3:1). The indications for operation were: infective valvulopathy in 14 cases, congenital aortic valve pathology in 23 cases and active native or prosthetic valve endocarditis in 53 cases. Follow-up data have been completed for 69 (76.7%) cases which have been echographically studied and the results have been analyzed on long-term period of time.

Pulmonary homografts of the 69 presented cases have been implanted in a subcoronary position in 60 cases whereas a mini-root or total root replacement in was performed in nine cases.

2.2. Classification of the homografts

According to the donor category PHGs have been classified in two groups: in group 1 were the pulmonary hypertension homografts (46 cases), where the PHGs were with the thickened cusps, procured from a recipients of the heart/heart-long transplantation; in group 2 were the normal pulmonary artery pressure pulmonary homografts (23 cases), where the PHGs had macroscopically normal cusps, procured from the multiorgan donors (MOD) or cadavers.

2.3. FU data

The implanting surgeons and/or cardiologists were requested to send us clinical and echocardiographic follow-up findings on regular basis (every 6 months to 1 year). Mean FU was 36.9 months (range, 2.5–88 months) for group 1, and 41.3 months (range, 7–88 months) for group 2. The size of the implanted valves was between 16 and 30 mm with the majority between 23 and 25 mm. Seventy-nine percent were between 21 and 28 mm (Fig. 1).

Significant echography changes were defined as a stenosis with the pressure gradient of >30 mmHg and/or insufficiency of >2/4.

All explanted PHGs have been sent back to the EHB for histological examination.

2.4. Statistical analysis

Statistical analysis was performed using Kaplan–Meier survival curves. Differences in prevalence are calculated by the Log-Rank test ($P > 0.05$).

3. Results

Follow-up was available in 69 cases (76.7%): 46 of group 1 and 23 of group 2. Five patients, three from group 1 and two of group 2, have been excluded from the study because of early explantation (technical problems or early massive valve incompetence). Fourteen of 43 homografts of group 1 (32.6%) and seven from 21 of group 2 (33.3%) have been explanted after 2.5–88 and 7–88 months, respectively. The main reasons of explantation were massive homograft regurgitation as a result of recurrence of endocarditis, cusp devitalization, cusp perforation or calcification of the PHG in both groups. Five cases (four of group 1 and one of group 2) had recurrence of endocarditis, seven cases (five of group 1 and two of group 2) had cusp devitalization, six cases (three homografts of each group) had cusp perforation, while four cases (one of group 1 and three of group 2) had cusp calcification (Table 1). All explanted PHGs had at the last echography examination massive regurgitation with or without heart decompensation. Almost all explanted homografts were sent back to the EHB for histological examina-

Fig. 1. Diameters of the pulmonary homografts (79% were between 21 and 28 mm).
tion. This showed essentially wear and tear induced lesions of the homograft leaflets [19].

On the FU echography study 19 of 43 cases of group 1 (44.18%) and 11 of 21 cases of group 2 (52.38%), (including the 21 explanted valves: 14 of group 1 and seven of group 2) have shown significant echography changes after long-term period of implantation.

The relationship between explanted homografts regarding to the valve diameter was the following: one, ten and three homografts of the diameter category of 19–22, 23–26 and 27–30 mm have been explanted after 36, 4–88 and 29.5–88 months, respectively, in a group with pulmonary hypertension, compared with five and two homografts of diameter category 23–26 and 27–30 mm after 7–68 and 42–45 months, respectively, in a group with normal pulmonary pressure.

The homografts still implanted gave following echography results per diameter group: in perfect state were still four, eight and three homografts of the diameter category 19–22, 23–26 and 27–30 mm after 74–88, 36–80 and 60–70 months, respectively, in a group with pulmonary hypertension, compared with five and two homografts of diameter category 19–22, 23–26 and 27–30 mm, after 60–84, 37–60 and 27–52 months, respectively, in a group with normal pulmonary pressure. In the same group, significant echography changes showed two, ten and two homografts after 36–88, 50–88, 55–70 months, for diameter category 19–22, 23–26 and 27–30 mm, respectively, in a group with pulmonary hypertension, whereas two, three and two homografts of a diameter category 19–22, 23–26 and 27–30 mm, showed significant echography changes after 60–84, 27–60 and 27–52 months, respectively, in a group with normal pulmonary pressure (Fig. 2).

4. Discussion

Aortic valve replacement with human aortic valve allografts has demonstrated benefit because of the superior haemodynamic performance, excellent treatment for endocarditis, freedom from anticoagulation, very infrequent thromboembolic complications and good long-term durability [8,9,13–15]. However, shortage in aortic homografts because of limited number of donors and early atherosclerotic changes of the aortic valves, resulting in a very high rate of the discarded aortic homografts during the procurement [5,7,9], lead to searching for the other possibilities for LVOT reconstruction in young patients, patients with severe endocarditis and those with contraindication for anticoagulation.

Since the biomechanical studies of Gorczynski [3] and Gerosa [4] have proved that the pulmonary homograft can withstand higher mechanical stress in systemic circulation, and considering the excellent results of the pulmonary autografts on left position (Ross procedure) [1,2,10,16,17], many European Cardiac Surgery centres have used pulmonary homograft as an aortic valve substitute, considering this operation less invasive than the Ross procedure. On the other hand, a very similar morphology of the pulmonary with the aortic valve [20] was an argument more for establishing the use of the pulmonary homograft for reconstruction of the LVOT. Following the initial implantations, very good results on short and mid-term period have been published by Gerosa [4], Luppinetti [8] and Mair [18].

However, long-term studies of pulmonary homografts used for the LVOT reconstruction were not very satisfying [5,8,9] and most cardiac surgery centres have almost completely abandoned this method. Several studies have

Table 1
The main reasons of PHG explantationa

<table>
<thead>
<tr>
<th>FU completed</th>
<th>PHT+ (Group 1)</th>
<th>PHT− (Group 2)</th>
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<tbody>
<tr>
<td>Explanted PHG</td>
<td>14 (32.5%)</td>
<td>7 (33.3%)</td>
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<tr>
<td>Recurrent endocarditis</td>
<td>4 (9.3%)</td>
<td>1 (4.7%)</td>
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<tr>
<td>Cusp devitalization</td>
<td>5 (11.6%)</td>
<td>2 (9.5%)</td>
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<tr>
<td>Cusp perforation</td>
<td>3 (6.9%)</td>
<td>3 (14.3%)</td>
</tr>
<tr>
<td>Calcification</td>
<td>2 (4.6%)</td>
<td>1 (4.7%)</td>
</tr>
<tr>
<td>Explanted per size group</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>19–22 mm</td>
<td>1 (36 months)b</td>
<td>0b</td>
</tr>
<tr>
<td>23–26 mm</td>
<td>10 (4–88 months)b</td>
<td>5 (7–68 months)b</td>
</tr>
<tr>
<td>27–30 mm</td>
<td>3 (29.5–88 months)b</td>
<td>2 (42–45 months)b</td>
</tr>
<tr>
<td>Normal echography on FU</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>19–22 mm</td>
<td>4 (74–88 months)b</td>
<td>2 (60–84 months)b</td>
</tr>
<tr>
<td>23–26 mm</td>
<td>8 (36–80 months)b</td>
<td>3 (37–60 months)b</td>
</tr>
<tr>
<td>27–30 mm</td>
<td>3 (60–70 months)b</td>
<td>2 (27–52 months)b</td>
</tr>
<tr>
<td>Significant echo changes on FU</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>19–22 mm</td>
<td>2 (36–88 months)b</td>
<td>2 (60–84 months)b</td>
</tr>
<tr>
<td>23–26 mm</td>
<td>10 (50–88 months)b</td>
<td>2 (27–60 months)b</td>
</tr>
<tr>
<td>27–30 mm</td>
<td>2 (55–70 months)b</td>
<td>2 (27–52 months)b</td>
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a PHT−, normal pulmonary pressure; PHT+, pulmonary hypertension. Histologic examination showed essentially wear and tear induced lesions of the homograft leaflets.
b Months after implantation.
been published on the long-term behaviour of the pulmonary homografts. Following Mair [5] higher incidence of endocarditis has been noted in the PHG from the donors older than 50 years. Also higher incidence of the valve regurgitation early after implantation has been seen at this category of the homografts. According to his long-term results, there were not arguments for using of the PHGs in the LVOT any more.

MacCarthy showed a higher incidence of valve failure in case of pulmonary homograft, comparing to the aortic homograft and pulmonary autograft used as the aortic valve substitute [9]. According to his results, pulmonary homograft should be reserved only for the patients with bacterial endocarditis when the aortic homograft is not available, and he advocates the intra-aortic cylinder technique to minimize leaflet distension and achieve good coaptation.

Since a considerable number of the EHB cryopreserved PHGs have been implanted in the LVOT according to different indications, we have been studying the echographic behaviour of this group of the homografts during a period of 10 years. The pulmonary homografts have been divided in the two above-mentioned groups, according to the morphologic appearance on procurement and the type of the donor. Short- and mid-term results of this category of homografts have been earlier presented at the Meeting of the EACTS in Paris in 1995 and published in 1997 by this group of authors, and have shown different results [7], compared with the long-term results presented at this paper.

The distinction between the two groups has been made because of a spectrum of the donor pathology and, consequently, the haemodynamic conditions to which the valves are subjected. They are similar in cadavers and multiorgan donors, while completely different in transplantation cases. In fact, in transplantation cases the majority of the donor pathology involves a pulmonary hypertension, either active or passive, whereas this is not observable in cadavers and multiorgan donors [7].

Considering the different morphologic appearance of the PHGs subjected to pulmonary hypertension and those subjected to normal pulmonary pressure, a comparative short and midterm study of those two groups of cryopreserved homograft valves has shown that the PHGs subjected to pulmonary hypertension could be better than those subjected to normal pulmonary pressure, according to the physiologic circumstances related to pulmonary hypertension. These homografts showed indeed, better results for pulmonary hypertension group (group 1) on short and mid-term period of time (7 vs. 10%, 27 vs. 37.5% and 33 vs. 80 % echographic changes after 12, 24 and 36 months, respectively). Further FU echographic examinations of the implanted homografts have been done in the implanting centres, whereas the histologic studies of the explanted PHGs have been performed at the EHB [19]. Long-term FU of the implanted valves in the different centres have not proved our earlier predictions.

Although one should expect different behaviour of these two homograft valves, according to the different haemodynamic circumstances of the donors, no significant differences in durability and competence have been found in long-term echography FU. Moreover, the main reasons of explantation were similar for both groups.

So far we haven’t found in the literature any similar study which could be used as a comparative study with our results.
5. Conclusion

Contrary to our previous echocardiography study of midterm implants, the long-term follow up of the PHGs, implanted in the LVOT, did not show a better function of the homografts subjected to pulmonary hypertension than those with normal pulmonary pressure. The failure rate of both groups of the PHG is too high to justify their use for LVOT reconstruction.

The main finding after long-term implantation is homograft failure, related to wear and tear mechanisms.

Further echocardiography and histological studies of the explanted valves are required for remaining PHG implanted on the LVOT to conclude definitive outcome of these cryopreserved homografts.

6. Comment

This study has some limitations: (1) it shows quite poor completion of FU data. The main reason is that some of implanting centres didn’t accept participation in the study. The problem of poor FU data has been already discussed earlier at the last Symposium of the EHB: ‘10 Years Experience With EHB Homograft Valves & Arteries’ [21]; (2) the number of implanted allografts of this category for reconstruction of the LVOT was limited. Only 90 homografts of this category have been sent from our Institution to the European Cardiac Surgery centres.

References


Appendix A. Conference discussion

Dr M. Antunes (Coimbra, Portugal): Your initial study appeared to indicate that the differences between pulmonary and aortic homografts were the fact that pulmonary homografts were sustaining high pressures before. Your current work obviously puts that theory completely down. So what is it that makes the difference between pulmonary homografts and aortic homografts?

Dr Jashari: Actually the initial study was because of the different appearance of those homografts during the procurement, because one saw during the procurement that those valves had a difference in the thickness of the leaflets. The leaflets of the pulmonary homografts related to normal pulmonary pressure are thin while leaflets of the pulmonary homografts related to pulmonary hypertension are quite thick. And initially a lot of cardiac surgeons thought that if you implant pulmonary homografts which have thickened leaflets, maybe it is better for resisting the systemic pressure.

There were arguments to support this theory, because publications of Gerosa and Mair in early studies of the pulmonary homografts on left position were very positive, and that was actually the theory that supported us to study the behavior of those two groups of the homografts. Now we don’t think that there is any difference between both groups. According to the results of the echography FU and explant studies we see that those valves actually are not good to be implanted in the left position.

Dr T. Mesana (Marseille, France): You harvested your homografts from transplant patients. If these patients have severe pulmonary hyperten-
sion, they must be excluded for heart transplantation. Did you collect enough data from the participating centers to give us information about the level of hypertension in the donors at the beginning of the study?

**Dr Jashari:** No. The way we classified those two groups of the valves were actually appearance on the procurement and the type of the donor. So the pulmonary homografts were procured from explanted hearts from the patients who got a new heart, (heart transplant recipients) and all those homografts had actually thickened leaflets, while the homografts which were procured from the hearts which were rejected for implantation, had contractility, dilated ventricles etc. they were with a normal pulmonary pressure.

**Dr Mesana:** But you don’t have the exact level of hypertension?

**Dr Jashari:** We didn’t do it, no. We did not measure the pulmonary pressure of the donors of our homografts.

**Dr C. Yankah (Berlin, Germany):** The pulmonary homograft might be functionally good when the structural integrity is also well preserved. I would like to know whether you have histological studies with regard to structural differences by age and by hypertension, because, as we know, under hypertension you might have disarrayed collagen fibers as well as the elastin fibers, which might dictate the functional durability postoperatively. Do you have some data to support your argument that the cryopreserved pulmonary homografts are not suitable for the systemic circulation in contrast to pulmonary autografts?

**Dr Jashari:** No. I don’t have. In this study we’re not including histological and ultrastructural findings of the pulmonary homografts. Here we did only the echography FU of the homografts.

**Dr G. Luciani (Verona, Italy):** You had quoted one manuscript that supported the use of pulmonary homografts for LVOT reconstruction. Those were very early results, but I am sure you are aware there was a manuscript which followed that by 1 year or so in the same journal that demonstrated catastrophic results with pulmonary homografts, and it was relative to the same series and to the same surgeons performing the operations. So my question to you is, did you need an additional study to see that, to demonstrate that?

Now, keep in mind you are presenting here a series that has 76% follow-up, so the results reported here are possibly even worse if you add those patients you lost to follow-up. And both the series with the normal pressure in the PA and the series with pulmonary hypertension are demonstrating very worrisome results. Don’t you think one should just forget the pulmonary homograft for LVOT reconstruction and close this investigation line?

**Dr Jashari:** First, about follow-up data, actually we were handicapped because we couldn’t get the cooperation of all implanting centers. That was one handicap for us. And second, I don’t think that pulmonary homografts have any indication for implantation in the left position. According to our long-term FU echography results use of homografts for reconstruction of the LVOT is not justified.

**Dr D. Metras (Marseille, France):** Considering that the pulmonary autograft that functions with low pressure before being transferred into the aortic position has an excellent mid-term and long-term competence, don’t you think that this shows only that it is a question of viability and inevitable degeneration of the pulmonary homograft valves, whatever they are, in high or low pressure?

**Dr Jashari:** You know, a lot of publications after short-term implantation of the pulmonary homografts in left position gave excellent results, but the same authors after 6 or 7 years of implantation of those homografts did publications which actually gave very, very bad results on longer term. So I think the first 3 to 4 years after implantation of pulmonary homografts in left position is quite acceptable, but you cannot implant the valve for 3, 4 or 5 years. The authors which did the implantation of more than 100, 150 homografts in left position after 5 years gave results which were terribly bad. So I think this has to be forgotten. Better long-term results of the pulmonary autografts on the LVOT are probably due to the viability and time of the pulmonary autograft.