Geometric mismatch between homograft (allograft) and native aortic root: a 14-year clinical experience

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Received 11 December 2000; received in revised form 22 June 2001; accepted 22 June 2001

Abstract

Objectives: We evaluated the effect of homograft/native aortic root geometric matching and mismatching on valve survival and myocardial remodeling.

Methods: Between January 1, 1987 and March 2000, a total of 292 patients, aged 1.5–78 years (mean, 46.2 years), underwent freehand subcoronary aortic valve (AVR; n = 207) and root (ARR; n = 85) replacement with matched and mismatched cryopreserved homografts. All patients had pre- and postoperative two-dimensional Doppler echocardiographic studies. Two-hundred and forty-three survivors, excluding children with complete data on sizing, were followed at a total follow-up time of 1269 patient-years. Seventy percent received matched and 30% received mismatched aortic homografts. The homograft valve sizes ranged from 19 to 28 mm.

Results: Hospital death for elective first operation was 2.3%, and late death after a mean follow-up of 52 months was 7.9%. The patient survival at 14 years was 92 ± 2%. By linear regression analysis, matched homografts were equal to or 1–2 mm less than the native aortic annulus (r² = 0.73). The valve survival in patients with AVR and ARR was 72 ± 4 and 80 ± 8% at 14 years, respectively. The freedom from reoperation was 92 ± 5, 77 ± 4 and 48 ± 10% at 14 years for matched, oversized and undersized homografts, respectively (P = 0.001). The postoperative cardiac index of patients with 22 and 24 mm homografts was 3.8–4.1 l/min², and there was a regression of the left ventricular mass and end-diastolic diameter (P = 0.001). Conclusions: The aortic homograft offers an excellent long-term clinical result. A mismatched homograft is a risk factor for postoperative aortic incompetence, reinfection with pseudoaneurysmal formation and reoperation for the freehand subcoronary implantation technique during the first 7 years of the postoperative period. It is prudent therefore to avoid mismatched homografts and use rather a properly sized stentless xenograft if a root replacement is not indicated. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Aortic allograft; Geometric mismatch; Ventricular remodeling

1. Introduction

It is over 38 years now since Ross and Barratt-Boyes independently introduced the clinical use of the aortic homograft [1,2]. Improved techniques of homograft valve implantation, procurement, processing and cryopreservation [3–8] mandate a renewed interest in improving the clinical results by recognizing the importance of implanting a proper aortic homograft size to match the geometry of the recipient’s aortic root and of using a specific implantation technique.

The limited availability of aortic homografts might pose a situation at an emergency operation to implant a mismatched homograft valve. Early valve failure could result, and subsequently, the enthusiasm for the excellent clinical results of this relatively technical artistry achieved by others [3–6,9–13] might fade away. Other factors related to early homograft failure are immune response, especially at a young age, and the learning phase of homograft implantation [14,15].

The selection of a stentless aortic valve substitute and accurate sizing will have an impact on early and long-term valve performance and myocardial remodeling, as well as bringing about an improvement in the patient’s clinical and cardiac performance. The valve performance will be disturbed by non-structural deterioration, such as cusp rupture, leaflet prolapse or distortion, commissural displacement, central and paravalvular leak (all by technical errors), aortic root dilatation from progressive dilatation which is not a technical error, and a progressive loss of leaflet extensibility by structural deterioration [5,6,10,13].

The purpose of this report is to analyze our 14-year clinical results of freehand subcoronary aortic valve replacement (AVR) and aortic root replacement (ARR) with
cryopreserved homovital homografts with particular reference to sizing and homograft/native aortic root geometrical mismatch.

2. Materials and methods

Between 1 January 1987 and March 2000, a total of 292 patients, aged 1.5–78 years (mean, 46.2 years), underwent subcoronary AVR (n = 207) and ARR (n = 85, including 25 mini-roots) with cryopreserved homovital homografts. Twelve patients who had an intraoperative conversion to prosthetic valve implantation were not included in this study. Complete data on homograft sizing were available in 243 patients. Children were excluded in the study because of the potential risk for immune response related early tissue deterioration.

There were 216 males and 76 females. Two-hundred and eighteen patients had aortic incompetence, 22 had aortic stenosis and 52 had combined lesions. One-hundred and seventy-seven patients had active infective aortic roots (104 native and 73 prosthetic endocarditis). Of these, 119 had ring abscesses. Of the 115 sterile roots, 15 had a history of a previous healed endocarditis, four had homograft degeneration, 12 had prosthetic valve dysfunction due to valve thrombosis and recurrent paravalvular leaks, 29 had congenital bicuspid valves and one quadricuspid valve, and there were 59 patients with rheumatic/degenerative valves. The preoperative mean left ventricular end-diastolic diameter (LVEDD) was between 60.0 ± 12.5 mm in patients with aortic valve incompetence and the left ventricular (LV) mass was between 229.3 ± 16.1 and 269.2 ± 25 g in patients with aortic stenosis, respectively.

Matched homografts were implanted in 169 (70%) patients and were defined as an internally sized aortic homograft annulus of 2 mm less than or equal to the recipient aortic root annulus. Mismatched homografts were implanted in 74 (30%) patients and defined as internally sized aortic homografts 3 mm less (undersize, n = 46) and 3 mm larger (oversized, n = 28) than the recipient aortic root annulus. Among the 184 survivals, 125 matched and 59 mismatched (37 undersize, 22 oversized) homografts were selected for AVR, and 44 matched and 15 mismatched (nine undersize, six oversized) homografts for ARR.

All of the homografts were harvested from hearts of cardiac transplant recipients, or from hearts of multi-organ donors if they were deemed unsuitable for heart transplantation, under sterile conditions. The donor age ranged from 12 to 56 years, with a mean age of 40.8 years.

The implanted homograft valves were obtained from our institution-based bank in Berlin, Bio-Implant Service of Eurotransplant in Rotterdam, the European Homograft Bank in Brussels and the Homograft Bank in Barcelona. The size of homografts implanted varied between 19 and 29 mm (mean, 22.5 ± 3 mm). Hegar dilators were used to measure the internal diameter of the homografts within 2 mm. For the selection of proper homograft size, the host annulus size was measured preoperatively by a two-dimensional echocardiographic measurement.

The intraoperative measured native annulus sizes were compared and correlated with the preoperative measured host annulus sizes and the selected homograft sizes.

2.1. Preoperative echocardiographic prediction of annulus size of the homograft recipient for homograft selection

The homograft sizes selected on the basis of preoperative echocardiographic prediction were plotted against the intraoperative measured annulus diameter. By linear regression analysis, the matched homograft sizes were equal to or 2 mm less than the native annulus (r² = 0.73; P < 0.001). The estimations of the preoperative echocardiographic non-calciﬁed annular measurements for emergency operations correlated weakly with the intraoperative direct measurements (r² = 0.45; P < 0.001). The distensibility (percentage systolic/diastolic diameter change) of the annulus of non-calciﬁed aortic lesions was 2.5–5.8% (mean, 3.8%) as compared with 4.5–12% (mean, 7.5%) of a normal aortic root. Patients beyond the age of 50 years demonstrated a distensibility of 2.5–4.5%.

ABO blood group and Human Leucocyte Antigen (HLA) matching between homograft donors and recipients was not practiced in all patients because of logistic reasons. Homograft recipients did not receive immunosuppressive therapy.

The performance of the homografts was analyzed in 243 patients using the homograft/native aortic root geometric annulus mismatch as a risk factor for reoperation.

2.2. Surgical technique

All of the homograft valve implantations were performed through a median sternotomy with the aid of conventional cardiopulmonary bypass with moderate hypothermic perfusion at 30–32°C, and myocardial protection with cold crystalloid cardioplegic arrest was achieved by maintaining the myocardial temperature at 10–12°C.

A preselected and thawed aortic homograft valved conduit was prepared by trimming the proximal muscle to 5 mm below the valve and removing the attached anterior of the mitral valve if it was not needed for annulus enlargement.

2.2.1. The freehand subcoronary implantation (n = 207)

The homograft/native aortic root sizing was 2 mm less than or equal to the recipient annulus internal diameter. The implantation was carried out by two suture lines: the proximal line with continuous interrupted or mattress 4-0 Prolene while the homograft conduit was held outside the aortic root. The upper line was accomplished with each sinus of Valsalva scalloped or leaving the non-coronary sinus in place. The depth of the sinus scallop was determined by the distance between the coronary ostia and the proximal line. The commissural posts of a properly sized
Homograft valve were fixed 1 cm above the recipient’s commissures at the sino-tubular junction to facilitate 40–50% leaflet coaptation. The homograft was inserted in the natural position to restore the anatomic units of the aortic root. In seven patients, a homograft with its anterior mitral leaflet was used to enlarge the aortic annulus by extending the incision into the native anterior mitral leaflet as described by Manouguian [16] (Fig. 1).

2.2.2. ARR (n = 85 including 25 mini-roots)

Homograft/native aortic root sizing was equal to or 2 mm larger than the recipient aortic annulus internal diameter. Total ARR was performed when there was a gross deformity caused by endocarditis with annular abscess or aortic–ventricular discontinuity or a congenital anomaly. All necrotic tissues were excised and the homograft was inserted as a free-standing cylinder or mini-root between the LV outflow tract and the ascending aorta of the host. The proximal suture line was performed with 4-0 Prolene by continuous interrupted sutures at the segment of the annulus facing each sinus. The reimplantation of the coronaries was performed by the continuous interrupted suturing technique described by Ross and others [3,5–7,14]. The distal homograft conduit was tailored to match the geometry of the host ascending aorta using continuous interrupted sutures. In the mini-root technique, the homograft root was then loosely wrapped with the host ascending to avoid crimping of the aortic root and subsequent valve incompetence.

Additional cardiovascular surgical procedures were: replacement of the ascending aorta (n = 12), coronary artery bypass surgery (n = 13), mitral valve replacement (n = 8) or reconstruction (29), and tricuspid valve reconstruction (n = 4).

2.3. Follow-up patients and protocol

Follow-up patients were reviewed periodically either by DHZB cardiologists or by the patient’s own cardiologist, initially at 1, 3 and 6 months after homograft valve replacement and at yearly intervals thereafter. At each visit, in addition to the clinical assessment, chest X-rays, electrocardiograms and echocardiograms were obtained and analyzed.

Homograft valve regurgitation was described by color Doppler echocardiography and categorized as follows: grade 0 as no aortic insufficiency, grade I as mild, grade II as moderate and grade III as severe [17].

Follow-up was complete at reoperation and removal of the homograft valve, death with the homograft valve in place or at the last follow-up in survivors with their homograft valves in place.

Follow-up information was available for evaluation in 94% of patients. The maximum follow-up was 14 years and 2 months, and the mean was 52 months. At the latest postoperative evaluation, 81% of the patients were in New York Heart Association (NYHA) class I and 19% in class II clinically.

2.4. Data analysis

Patient survival and valve failure were analyzed with Kaplan–Meier curves, and the probability and standard

Fig. 1. Aortic annulus enlargement with extended incision into the native anterior mitral valve leaflet using a valved homograft with anterior mitral valve leaflet.
error were calculated. Continuous data were presented as means ± standard deviation (SD). Variables relating to the recipient, including age, sex, underlying aortic root pathology, homograft/patient aortic root annulus size and implantation technique, were analyzed using the Cox proportional hazards model. Linear regression techniques were applied to establish the relationship between host and homograft annular size.

The log-rank test was used to identify statistical significance as an endpoint analysis. Implantation of mismatched homografts and reoperation for homograft explantation, and patient survival in relation to a variable period of homograft operation (1987–1993, and 1994–2000) were included in the analysis.

At the echocardiographic studies, both M-mode recordings and off-line measurements were guided by the two-dimensional image. The ejection fraction was calculated according to Teichholz et al. [18] and the LV mass by means of the cube formula. Blood flow velocity in the LV outflow tract was estimated by pulsed wave Doppler from an apical four-chamber view (sample size of 5 mm). Pressure gradients were calculated according to the simplified Bernoulli equation (Doppler pressure gradient = 4 × (peak velocity)^2). The mean gradients were calculated from off-line planimetry of the continuous wave Doppler recordings [17–19].

Analysis of variance (ANOVA) was used to compare the differences between the three different valve sizes (match, undersize and oversize) and the pre- and postoperative values of LV mass and LVEDD. The results are presented with 95% confidence intervals (CI).

Homograft valve failure was diagnosed when there was an onset of postoperative evidence of clinically mild, moderate or severe valve stenosis or incompetence with or without conduit calcification. The time of censoring for significant valve stenosis or incompetence, or dysfunction due to structural or non-structural deterioration was the date of reoperation and homograft explantation, late death from the causes above, or the last follow-up for the remaining survivors.

3. Results

3.1. Patient survival

The hospital mortality for an elective first operation was 2.3%. Late death was 7.9% after a mean follow-up of 52 months.

On survival analysis, 92% of the hospital survivors are alive at 10 and 14 years after homograft valve replacement, respectively (Fig. 2). Mismatched homograft was not a risk factor for death in both periods of operation (risk ratio, 0.35; 95% CI, 0.10–1.23; P = 0.17).

3.2. Reoperation and valve survival

Homografts were explanted in 48 patients during the 14-year follow-up at a mean time interval of 2.5 years after implantation (Table 1). Forty-one (85.5%) patients received the freehand subcoronary implantation technique and seven (14.5%) had the root replacement technique. The age of these patients at the first homograft operation was 40.1 years (SD, ±19.7 years). Of the 48 (20%) reoperations, eight (seven AVR, one ARR) were due to persistent infection (3% of endocarditis patients) with pseudoaneurysmal formation or reinfection (1% of endocarditis patients).

The freedom from explantation of the homografts in patients with ARR at 13 years is 88%, while in the two operation periods, the use of undersized homografts was significantly different (P = 0.003).

3.3. Homograft/native aortic root mismatch

The probability of homograft valve survival for geometric oversized homografts was 92 ± 6%, 77 ± 4% for matched homografts and 48 ± 10% for undersized homografts at 13 years (P = 0.001; Fig. 4; Table 1). The P value for the log-rank test adjusted for the two periods of operation (1987–1993, and 1994–2000) was 0.33.

Table 1

<table>
<thead>
<tr>
<th>Determinants of homograft reoperation</th>
<th>Risk ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>1.922</td>
<td>0.803–4.601</td>
<td>0.14</td>
</tr>
<tr>
<td>Age &gt;30 years</td>
<td>0.9907</td>
<td>0.9575–1.025</td>
<td>0.59</td>
</tr>
<tr>
<td>Undersize</td>
<td>2.975</td>
<td>1.432–6.184</td>
<td>0.001</td>
</tr>
<tr>
<td>Oversize</td>
<td>0.361</td>
<td>0.081–1.599</td>
<td>0.16</td>
</tr>
<tr>
<td>Match</td>
<td>0.587</td>
<td>0.297–1.161</td>
<td>0.12</td>
</tr>
<tr>
<td>Freehand AVR</td>
<td>2.033</td>
<td>0.85–4.858</td>
<td>0.11</td>
</tr>
<tr>
<td>ARR</td>
<td>0.492</td>
<td>0.206–1.176</td>
<td>0.11</td>
</tr>
<tr>
<td>Aortic ring abscess</td>
<td>1.318</td>
<td>0.671–2.588</td>
<td>0.42</td>
</tr>
</tbody>
</table>
homograft operation (1987–1993 and 1994–2000) was 0.003.

Twenty-four patients with the freehand subcoronary implant were reoperated on due to mismatched (22 undersized, two oversized) homografts. Thirteen developed aortic incompetence grade III (three leaflet prolapses, ten central leaks), and there were 11 patients with incompetence grade II and a mean gradient of more than 5 mmHg (three cusp ruptures, three paravalvular and seven central leaks). Dysfunctions of matched homografts encountered in the freehand technique group were due to valves inserted in a native root with a geometric disparity between the annulus, sinus of Valsalva and the sino-tubular junction and distorted infected native annulus. Among the ten patients who received mismatched homografts (eight undersized, two oversized) for root replacement with the mini-root technique, two developed a mean transvalvular gradient of over 5 mmHg and eight others below 5 mmHg. One patient developed recurrent endocarditis. The geometric disparity between the homograft and the native root was at subannular, annular and sino-tubular levels.

3.4. Matched homografts

The valve performance was excellent in 155 (91.7%) patients. Fourteen (8.3%) patients, including patients with acute aortic root endocarditis and abscesses and a Marfan patient, developed valve dysfunction due to paravalvular ($n = 2$) and central leaks ($n = 12$, including five with the mini-root technique) because of technical reasons. One patient developed homograft endocarditis with valve incompetence. The freedom from valve explantation for all causes was $77 \pm 4\%$ at 10 and 14 years (Fig. 4).

3.5. Correlation between homograft size and patient body surface area

Hemodynamically, there was no disparity between the patient’s body surface area and the cardiac output for the selected homograft size. For the 22 mm homograft valves, the mean cardiac index measured postoperatively was $4.09 \pm 0.5$ (95% CI of 3.62 and 4.55 l/m$^2$), and for a 24 mm valve, the mean cardiac index was $3.8 \pm 0.4$ (95% CI of 3.40 and 4.2 l/m$^2$). Two patients with a mini-root technique and an undersized homograft demonstrated cardiac indices of 2.7 l/m$^2$.

3.6. Left ventricular remodeling

The postoperative LV remodeling was achieved by reduction of the LV mass (g) for aortic stenosis and the LVEDD (mm) for aortic incompetence. Over a period of 6–60 months, the LV mass reduced by 12–15% and the LVEDD by 10–12%. The aortic annulus diameter of patients, particularly with annuli greater than 27 mm, remained stable without calcification and progressive dilatation.

3.7. Thromboembolism

Our patients were treated with aspirin for 3 months after surgery and have not been complaining of symptoms related to thromboembolic complications, either in the early or late postoperative follow-up periods.

4. Discussion

The anatomic units of the aortic homograft are distensible by 8–12% and will result in the radial movement of the commissures outward, even if the aortic annulus is fixed and inexpansible. In a normal non-calciﬁed aortic root, a 16% change in the aortic root radius would allow the leaflet edges to straighten in the systole and form a triangular orifice [15,20].

Accurate matching of a homograft to the host aortic root either equal to or 2 mm less than the host annulus at subcoronary implantation will therefore provide over 50% leaflet coaptation and excellent long-term clinical and hemodynamic performance which is identical to that of ARR [4–6,9,11,21].

The less distensible stentless xenografts, which appear to be complimentary, rather than a competitive valve substitute to the homograft, require oversizing by 2–3 mm to
allow proper matching to a distensible native aortic root in order to maintain over 50% leaflet coaptation.

Besides patients’ special wishes and a contraindication for long-term anticoagulation, the principal indication for ARR in our series was acute endocarditis with burrowing ring abscess. Sepsis and NYHA functional classes III and IV were major risk factors for early death in this group of patients.

Twenty-seven (56.3%) homograft early and late failures in our series were associated with geometric mismatching, and of the matched homografts, 14 (29.2%) failures were technical and seven (14.5%) were due to infection. In our series, cryopreserved homovital homograft valve explantation occurred frequently in the first 7 postoperative years due to structural deterioration in most patients with mismatched homografts. However, the valve performance of matched and oversized homografts remained stable after 2 and 5 years until 14 years postoperatively, respectively (Fig. 4; \( P = 0.001 \)). Similar clinical results have been reported by others [4,6,11].

In small aortic roots or in subvalvular obstructive lesions, it seems prudent to enlarge the aortic root to accommodate a larger aortic homograft. The aortotomy is made through the sinotubular level. Subsequently, non-structural valve failure, such as cusp rupture, leaflet prolapse or distortion, paravalvular leak pseudoaneurysm formation and commissural displacement, resulting in a central leak, occurred. An ongoing loss of leaflet flexibility and expansibility, such as structural deterioration, may be associated with an undersized valve, as could be demonstrated, particularly in adult patients.

In most patients, despite homograft/native root geometric mismatch, there was no mismatch between the cardiac output and the patient’s surface area as demonstrated in the postoperative measurements of the cardiac indices. Like other reports, a regression of LV hypertrophy and LVEDD could be achieved over a period of 6–60 months [12,13,22–24]. Reduction of LV hypertrophy, LVEDD and improvement of the ventricular performance underscore the hemodynamic superiority of a non-obstructive stentless bioprostheses over a stented bioprostheses of the same size [25]. It is possible therefore to have a relatively small homograft valve (up to 3 mm smaller) without a demonstrable gradient. The gradient to valve area was not studied in this series. Rahimtoola, however, underlines that the relationship of the gradient to valve area is curvilinear, and once the effective orifice size of the aortic valve is critically reduced to less than 35% of normal, the gradient rises precipitously [24,25]. We encountered this in two patients with mini-root and 13 patients with subcoronary implantations.

The multivariate analysis identified undersized homografts as a risk factor for developing aortic valve incompetence, early and late recurrent endocarditis in the freehand subcoronary implantation technique. Due to standardization of the homograft sizing technique at the beginning of homograft implantation at our institution, the use of mismatched homografts was not specifically associated with surgical inexperience or a particular period of implantation, but rather with availability. Mismatched homografts were rather frequently used at emergency operations for complicated acute infective endocarditis, and the number of implanted matched and mismatched homografts was evenly distributed in the two operation periods (1987–1993 and 1994–2000). The \( P \) value of reoperation for explantation of mismatched homografts for the log-rank test adjusted for both implantation periods was 0.003. The use of mismatched homografts, therefore, was not associated with surgical inexperience, but rather, with the availability of proper homograft sizes at the time of emergency operations in both operation periods. Although the risk for reoperation was twice as high in the second operation period (risk ratio, 2.05; 95% CI, 1.07–3.90; \( P = 0.028 \)), it was demonstrated that mismatched homografts did not have an adverse effect on patient survival, and therefore were not a risk factor for death for both operation periods (risk ratio, 0.35; 95% CI, 0.10–1.23; \( P = 0.17 \)).

The durability of the homografts achieved with both implantation techniques therefore was influenced by sizing and the implantation technique as demonstrated in the valve survival analysis in Fig. 3 and by others [6,9,11,12,14,21]. However, a mini-root technique should not be used as a standard root replacement technique because of its potential to develop valve incompetence from crimping the homograft following wrapping with the native aortic root. Furthermore, it can complicate root fibrosis with subsequent late calcifica-
tion as well as coronary ostial stenosis leading to reoperation. The technique can, however, be beneficial for local root hemostasis, and therefore can be used in selected groups of patients and as a rescue procedure to save patients from catastrophic bleeding and prolonged operation times.

5. Conclusions

The identical excellent long-term hemodynamic performance of cryopreserved homograft valves used for AVR and ARR techniques is associated with proper sizing and meticulous implantation techniques.

Geometric mismatch between the native and homograft root was not a risk factor for postoperative death, but it was a risk factor for postoperative aortic incompetence, reinfec-
tion with pseudoaneurysmal formation and reoperation in patients with a freehand subcoronary implantation technique and a common hazard for the mini-root implantation technique in the first 7 years after operation. The use of mismatched homografts was not associated with surgical inexperience, but rather, was associated with the availability of the proper homograft size at the time of emergency operations. In a situation where there is only a mismatched homograft available, it seems therefore prudent to choose a stentless xenograft as an alternative biological valve substitute, which is readily available in all sizes, to restore the anatomic and functional units of the patient’s aortic root and to achieve a competent valve.

Acknowledgements

The authors wish to thank Mrs Stein for her statistical assistance.

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