Hemodynamic Performance of Cryopreserved Aortic Homograft Valves During Midterm Follow-Up

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Objectives. The aim of this prospective study of adult patients operated with a cryopreserved aortic homograft was to use serial echocardiographic data to evaluate the postoperative hemodynamic performance of these valves.

Background. Only limited data on hemodynamic performance of aortic homografts at rest and during exercise are available. Controversy also exists regarding incidence and progression of aortic regurgitation (AR).

Methods. Fifty-nine patients aged 39–86 years who received an aortic homograft (median size 21 mm) implanted with subcoronary technique were studied with serial Doppler-echocardiography (D-E). In 31 of these patients, D-E also was performed during supine exercise.

Results. Overall survival was 100% during a median follow-up of 28 months (range 4–54). During follow-up AR grade II or more was detected in 25% of the patients with an increasing time-related risk of developing AR. Maximum and mean pressure differences at 7 months follow-up calculated with the short form of the Bernoulli equation were 11.4 (4.6) and 5.5 (2.1) mm Hg, respectively. During supine exercise that increased cardiac output 72%, maximum pressure difference increased from 11.9 (5.2) to 18.5 (9.5) mm Hg.

Conclusions. The aortic homograft valve shows low pressure differences at rest and during exercise, but AR grade I or II is often seen during follow-up. As AR progresses with time we stress the importance of echocardiographic follow-up of patients with aortic homografts.

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The use of aortic homografts for aortic valve replacement was pioneered by Ross (1) and Barratt-Boyes (2) in the early 1960s. Theoretically, the freehand implanted valves with preserved aortic root function and a nonobstructed central flow offer superior flow dynamics compared with mechanical valves or stented bioprostheses. Clinical results with aortic homograft valves are well documented, but currently limited data on hemodynamic performance are available (3–11). It is known that patients with an aortic homograft may develop various degrees of aortic regurgitation (AR), depending on several variables such as preservation method, structural degeneration and implantation technique (3–11). However, controversy still exists regarding incidence, severity and progression of AR.

The aim of this prospective study was to evaluate the hemodynamic performance of cryopreserved subcoronarily implanted aortic homografts, with Doppler echocardiography (D-E) at rest and during increased flow rates induced by supine exercise. In this study, we also present clinical results and an analysis of the incidence and progression of AR.

Methods

The study was approved by the Committee of Ethics of Karolinska Hospital and informed consent was obtained from all patients.

Study patients. The study group consisted of 59 consecutive patients, 33 men and 26 women with a mean age of 68 years (range 39–86), who underwent aortic valve replacement with an aortic homograft between March 1993 and December 1996. The indication for surgery was aortic stenosis in 44 patients (75%), regurgitation in 8 (13%) and mixed lesion in 7 (12%). An aortic homograft valve was selected in cases of absolute or relative contraindications to anticoagulant treatment or if the patient expressed a strong wish to avoid anticoagulation or a wish to receive a homograft. Preoperatively, 35 patients (59%) were in NYHA functional class III or IV.

Homograft preparation. All homografts were harvested within 24 h of donor death. The grafts were kept in +4°C Ringer’s solution and dissected under sterile conditions at the Homograft Bank of the Karolinska Hospital. The valves were kept in a solution of broad-spectrum antibiotics in 250 mL tissue culture medium 199 at +4°C for another 24 h. After rinsing in tissue culture medium, 10% dimethyl sulfoxide was
added and the valves were then cryopreserved at a rate of 
−1°C/min to −40°C. After further cooling to −100°C the 
valves were transferred to permanent storage in liquid nitro-
gen. The preparation and preservation technique has previ-
ously been described in detail by Lange and Hopkins (12). Thawing in three consecutive +40°C baths of Ringer’s solution 
was done in the operating room during the initial stage of the 
operation.

**Operative procedures.** The operations were performed 
during cardiopulmonary bypass at 32°C hypothermia. Myocar-
dial protection was accomplished with intermittent cold blood 
retrograde cardioplegia via the coronary sinus. All valves were 
inserted as freehand homografts in the subcoronary position 
(13). We selected homografts with 2 mm less annular diameter 
than that of the recipient aortic annulus, as measured at 
preoperative echocardiography and/or with an obturator dur-
ing the operation. The grafts were implanted with a two-
suture-line technique without rotation and the noncoronary 
sinus was not tailored down to the base of the leaflet. Inter-
rupted sutures were used proximally and a continues running 
suture finished the distal suture-line. A mattress 3-0 braided 
suture tied over a felt pledget on the outside of the aortic wall 
was used to position the tops of the commissural pillar approx-
imately 5–10 mm downstream of the native commissural rem-
nants. One patient received a 17-mm homograft valve; 7, 
patients an 18-mm valve; 8, a 19-mm valve; 9, a 20-mm valve; 
14, a 21-mm valve; 4, a 22-mm valve; 9, a 23-mm valve; 2, a 
24-mm valve; 4, a 25-mm valve; and 1, a 27-mm valve. The 
last patient, with a native aortic root diameter of 29 mm had 
expressed a strong wish to receive a homograft. Concomitant 
coronary bypass grafting was performed in 22 patients (37%), 
mitril valvuloplasty in 1 patient and myectomy of the septum 
in another.

**Doppler echocardiography.** Transthoracic Doppler echocar-
diography was performed by one of two experienced oper-
ators (MJE or VR) using Acuson 128 XP/10 ultrasound 
equipment (Mountain View, CA, USA) with 2–2.5 MHz 
imaging and nonimaging transducers. The first D-E was per-
formed within one week of surgery, before hospital discharge. 
Two subsequent examinations were done within the first 
postoperative year and yearly thereafter. On each occasion 
complete color, pulsed-wave and continuous-wave D-E was 
carried out including two-dimensional measurements.

To obtain the maximum velocity across the homograft 
(V_AO), continuous Doppler was used from different transducer 
positions. The flow velocity in the left ventricular outflow tract 
(V_LVOT) was recorded with pulsed Doppler from the apical 
view, approximately one cm proximal to the aortic prosthesis, 
before acceleration of the flow occurred. Maximum (ΔP_max) 
and mean (ΔP_mean) Doppler-derived pressure differences were 
calculated from V_AO using the short [ΔP = 4 × V_AO^2] and the 
long form [ΔP = 4 × (V_AO – V_LVOT)] of the modified 
Bernoulli equation (14). The effective orifice area (EOA), 
stroke volume (SV), cardiac output (CO) and aortic valve 
volume flow (AVF = SV/Systolic Ejection Period) were calcu-
lated (15). Ejection fraction (EF) was determined using the 
Simpson rule (16). Aortic regurgitation was estimated as trivial 
 grade I), mild (grade II) moderate (grade III) and severe 
(grade IV), based on the information from color flow mapping, 
pulsed-wave Doppler and continuous-wave Doppler (17–19).

All measurements are presented as the average of three 
consecutive cardiac cycles in patients with sinus rhythm and 
five consecutive cycles in patients with atrial fibrillation. Mea-
urements and calculations, including the grading of AR, were 
made on-line, with the operator unaware of the results of previous 
examinations.

**Exercise echocardiography.** At a mean follow-up of 7 
months, 31 of the patients, with a median valve size of 21 mm, 
performed a symptom-limited supine bicycle exercise test. For 
this purpose, we used a special bicycle ergometer with a 
possibility of left lateral tilt to facilitate ultrasound measure-
ments (Ergoline GmbH & Co KG, Bitz, Germany). The initial 
workload was 20 or 30 W depending on age, sex and fitness. 
The work load was increased in steps by 10 or 20 W every 
3 min. The exercise test was interrupted at perceived exertion 
grade 7/10, according to the Borg scale (20). Heart rate and 
Doppler recordings across the aortic prosthesis and in the left 
ventricular outflow tract were obtained during the last minute 
at each level of work load, using the same acoustic windows as 
for the rest studies. Ten good-quality Doppler curves were 
traced at each load and the measurements were averaged. The 
diameter of the left ventricular outflow tract at rest was used to 
calculate SV during exercise. Valve area index (EOA at 
rest/BSA) was calculated for all patients undergoing exercise 
and a prosthesis-patient mismatch was considered present 
when values <1cm²/m² were obtained (21). Calculations from 
exercise studies were made off-line from videotapes using the 
same equipment and the same software as for resting studies.

The coefficients of variation for inter- and intraobserver 
measurement variability for the experienced operators at our 
laboratory have been reported earlier and are 2.0% and 2.1% 
for aortic velocity measurements at rest and 2.0% and 1.9% for 
aortic velocity measurements during exercise. For measure-
ment of LVOT diameter the corresponding values are 3.9% 
and 2.8%, respectively (22). Intraobserver variability for grad-
ing of AR was assessed in 39 registrations chosen at random, 
with excellent agreement according to Kappa statistics (Kappa
value $0.92 \pm 0.05SE$). Disagreement in grading of AR between the two blinded readings occurred in two cases and regarded only AR grade I and II.

**Statistics.** Continuous data are presented as mean and one standard deviation (SD). The Kaplan-Meier product limit estimate of survivor function was employed to calculate the actuarial incidence of postoperative aortic homograft regurgitation (23). Three patients who developed AR grade III/IV were reoperated on and then censored from further survival analysis. The instantaneous risk of aortic regurgitation was described with the hazard function (24). One-way analysis of variance (ANOVA) was used to study the difference in Doppler-derived variables between patients divided according to valve size. When the F-value revealed a significant difference, the means were compared with Scheffe’s test. Two-way ANOVA for repeated measures, paired or unpaired t test and regression analyses were used where appropriate. A p value $<0.05$ was considered as significant.

**Results**

There was no mortality during a median clinical follow-up time of 28 months (range 4–54). One 81-year-old patient suffered a minor stroke 30 days after the operation. There was no evidence of endocarditis in any patient, although 1 patient was treated for septicemia. Three patients deteriorated during follow-up from NYHA functional class I to class III due to AR grade III or IV and required reoperation. At the most recent follow-up, 54 of the remaining 56 patients (96%) were in NYHA class I or II and 2 patients were in class III. Overall freedom from reoperation was 94%.

**Homograft valve regurgitation.** The median echocardiographic follow-up was 25 months (range 4–50). In 6 patients (10%), AR grade I was demonstrated by D-E 1 week after the operation. During follow-up AR increased in severity to grade II-IV in 5 of these 6 patients and necessitated reoperation in two cases. Actuarial analysis of freedom from AR more than grade I, II and III, respectively, is shown in Figure 1. During follow-up, AR grade II or more was detected in 25% (15/59) of the patients. The hazard function showed a time-related increasing risk of developing AR, which at two years was 1.7 for AR grade I or more, 0.4 for grade II or more and 0.06 for AR grade III or more (Fig. 2).

To study the hemodynamic effect of AR grade II, the left ventricular end-diastolic diameter (LVD) and systolic function were analyzed. LVD at the most recent follow-up was 4.8 (0.6) cm in patients with AR grade II ($n = 12$) and 4.7 (0.4) cm in AR grade 0-I ($n = 44$). LVD did not change significantly during follow-up within the groups. The mean difference in LVD from 1-week examination to the most recent follow-up was 0.16 (0.5) cm in patients with AR grade II and $-0.10$ (0.6) cm in those with AR grade 0-I ($p = 0.19$). There was no significant change in EF during follow-up in any of the groups.

**Reoperations.** The 3 patients who developed regurgitation grade III or IV were uneventfully reoperated on at 4, 18, and 26 months, respectively, with implantation of a mechanical prosthesis. In one of these patients the 23-mm homograft suddenly failed 4 months after implantation and required valve explantation. Small fenestrations were observed at the coaptation zones of the leaflets which might have caused leaflet prolapse. In the second and third patients (valve size 18 mm and 21 mm), AR progressed during the first and second postoperative year due to prolapse of the left and noncoronary cusps, respectively. On reoperation, no macroscopic signs of structural degeneration of the homografts were seen. Microscopic examination revealed nonspecific degenerative tissue

![Figure 1. Actuarial analysis of freedom from postoperative aortic regurgitation (AR) more than grade I, II and III, respectively, in 59 patients with a cryopreserved aortic homograft valve. Numbers of patients at risk and 95% confidence limits are indicated.](image-url)
changes with fissures and splitting of elastic fibers in all three explanted homograft valves.

**Hemodynamics at rest.** Hemodynamic findings at a mean follow-up of 7 months were compared with those at one week (Table 1). Stroke volume was significantly higher at the follow-up. There was no significant change in EF, EOA or CO, while heart rate, \(D_P^{\text{max}}\) and \(D_P^{\text{mean}}\) decreased slightly during the same period. Doppler-derived variables for all valve sizes at 7 months follow-up are presented in Table 2. EF and CO were similar in all groups. There was a significant negative correlation between \(D_P^{\text{max}}\) and valve size (\(p < 0.01, r = -0.37\)). However, a considerable overlap in pressure differences across the prostheses existed between the four groups of valve sizes, and a statistically significant difference in \(D_P^{\text{max}}\) and \(D_P^{\text{mean}}\) was found only between 17–19 mm valves and 22–23 mm valves. The group with 17–19 mm valves also differed significantly from all other sizes regarding EOA.

**Hemodynamics during exercise.** We obtained satisfactory Doppler recordings in all the 31 patients. All but 2 patients had sinus rhythm. Median achieved workload during the symptom-limited supine exercise test was 60 W (range 30–150). In 28 patients exercise capacity was limited by leg fatigue and in three by dyspnoea. None of the patients developed chest pain. Hemodynamic changes during exercise are presented in Table 3. The increase in CO was effected mainly by an increase in heart rate by 59% and a smaller, but significant, increase in stroke volume by 7%. \(D_P^{\text{max}}\) and \(D_P^{\text{mean}}\) calculated with the short form of the Bernoulli equation, increased by 6.6 mm Hg and 3.0 mm Hg, respectively, during exercise (\(p < 0.001\) versus rest). EOA did not change significantly.

**Table 1.** Aortic Homograft Valves: Hemodynamic Results in 57* Patients 1 Week and 7 Months Postoperatively

<table>
<thead>
<tr>
<th>Variable</th>
<th>1 week</th>
<th>7 months</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>79 (13)</td>
<td>72 (14)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>LVD (cm)</td>
<td>4.8 (0.6)</td>
<td>4.7 (0.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>60 (14)</td>
<td>60 (9)</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke volume (mL)</td>
<td>60.7 (13.4)</td>
<td>68.0 (13.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>4.7 (1.1)</td>
<td>4.8 (1.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Maximum velocity LVOT (m/s)</td>
<td>1.0 (0.14)</td>
<td>0.95 (0.14)</td>
<td>NS</td>
</tr>
<tr>
<td>Maximum velocity Ao (m/s)</td>
<td>1.8 (0.4)</td>
<td>1.7 (0.3)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>(D_P^{\text{max}}) (mm Hg)</td>
<td>13.2 (6.2)</td>
<td>11.4 (4.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(D_P^{\text{max}})† (mm Hg)</td>
<td>9.1 (5.9)</td>
<td>7.7 (3.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(D_P^{\text{mean}}) (mm Hg)</td>
<td>6.8 (3.1)</td>
<td>5.5 (2.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(D_P^{\text{mean}})† (mm Hg)</td>
<td>4.5 (2.8)</td>
<td>3.5 (1.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Effective orifice area (cm²)</td>
<td>2.1 (0.6)</td>
<td>2.1 (0.5)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are shown as mean (one SD). *One reoperated patient was excluded and another was unable to come to both examinations. Ao = aorta; LVD = left ventricular end-diastolic diameter; LVOT = left ventricular outflow tract. \(D_P^{\text{max}}\) and \(D_P^{\text{mean}}\) = maximum and mean pressure differences calculated with the short and the long (†) form of the Bernoulli equation.

**Table 2.** Aortic Homograft Valves: Results by Annulus Diameter in 57* patients 7 Months Postoperatively

<table>
<thead>
<tr>
<th>Valve size</th>
<th>Variable</th>
<th>17–19 mm (n = 16)</th>
<th>20–21 mm (n = 22)</th>
<th>22–23 mm (n = 12)</th>
<th>24–27 mm (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSA (m²)</td>
<td></td>
<td>1.7 (0.2)</td>
<td>1.9 (0.2)</td>
<td>2.0 (0.2)</td>
<td>2.0 (0.2)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td></td>
<td>63 (9)</td>
<td>59 (10)</td>
<td>53 (9)</td>
<td>64 (6)</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td></td>
<td>4.5 (0.8)</td>
<td>5.0 (0.9)</td>
<td>4.5 (1.5)</td>
<td>5.6 (1.0)</td>
</tr>
<tr>
<td>(D_P^{\text{max}}) (mm Hg)</td>
<td></td>
<td>13.9 (4.7)</td>
<td>11.8 (4.4)</td>
<td>8.7 (3.7)</td>
<td>9.4 (3.3)</td>
</tr>
<tr>
<td>(D_P^{\text{max}})† (mm Hg)</td>
<td></td>
<td>9.7 (4.2)</td>
<td>7.9 (4.0)</td>
<td>5.6 (3.1)</td>
<td>6.2 (2.0)</td>
</tr>
<tr>
<td>(D_P^{\text{mean}}) (mm Hg)</td>
<td></td>
<td>6.5 (2.0)</td>
<td>5.6 (2.3)</td>
<td>4.2 (1.6)</td>
<td>4.7 (1.5)</td>
</tr>
<tr>
<td>(D_P^{\text{mean}})† (mm Hg)</td>
<td></td>
<td>4.2 (1.8)</td>
<td>3.6 (2.0)</td>
<td>2.6 (1.4)</td>
<td>2.8 (1.1)</td>
</tr>
<tr>
<td>Effective orifice area (cm²)</td>
<td></td>
<td>1.7 (0.3)</td>
<td>2.3 (0.4)</td>
<td>2.5 (0.3)</td>
<td>2.7 (0.3)</td>
</tr>
</tbody>
</table>

Values are shown as mean (one SD). *One reoperated patient was excluded and another was unable to come to the examination. \(D_P^{\text{max}}\) and \(D_P^{\text{mean}}\) = maximum and mean pressure differences calculated with the short and the long (†) form of the Bernoulli equation.
Table 3. Aortic Homograft Valves: Results at Rest and at Peak Symptom-limited Supine Exercise in 31 Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>Exercise</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beat/min)</td>
<td>71 (10)</td>
<td>113 (20)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>139 (21)</td>
<td>184 (33)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke volume (mL)</td>
<td>67.8 (13.8)</td>
<td>72.5 (14.2)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>4.7 (0.9)</td>
<td>8.2 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Maximum velocity LVOT (m/s)</td>
<td>9.0 (1.1)</td>
<td>11.2 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Maximum velocity Ao (m/s)</td>
<td>1.7 (0.5)</td>
<td>2.1 (0.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Aortic valve volume flow (mL)</td>
<td>227 (40)</td>
<td>280 (64)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Values are shown as mean (one SD). Ao = aorta; LVOT = left ventricular outflow tract; \( \Delta P_{\text{max}} \) and \( \Delta P_{\text{mean}} \) = maximum and mean pressure differences calculated with the short and the long (†) form of the Bernoulli equation.

Eight of the 31 patients studied during exercise fulfilled the criterion for prosthesis-patient mismatch (valve area index range 0.76–0.98 cm\(^2\)/m\(^2\)). Homograft sizes in these eight patients ranged from 18 mm to 24 mm. There were 2 patients with an 18-mm valve, 2 with a 19-mm valve, 2 with a 21-mm, 1 with a 22-mm valve and 1 with a 24-mm valve. The difference between the annulus size of the patient and the homograft annulus size did not differ significantly (p = 0.2) between the group with “mismatch” (mean difference 1.6 ± 0.5 mm) and without “mismatch” (mean difference 2.0 ± 0.9 mm). Furthermore, the two groups did not differ regarding EF, CO, AVF or achieved workload. The “mismatch” group showed significantly higher pressure differences at rest (p < 0.001) and at peak exercise (p < 0.001), and a significantly higher increase of \( \Delta P_{\text{max}} \) during exercise than the group without “mismatch” (Fig. 3). There was a significant interaction according to two-way ANOVA between the groups and the effect of exercise (F(1,29) = 21.2, p < 0.001). The difference in \( \Delta P_{\text{max}} \) calculated with both forms of the Bernoulli equation, between the two groups was significant even after adjustment for differences in homograft valve sizes (p < 0.001 at rest, p < 0.001 at peak exercise).

**Discussion**

This study confirmed all recognized advantages of aortic valve replacement with cryopreserved aortic homografts, demonstrating the low incidence of thromboembolic events and homograft endocarditis, and low pressure differences across the valves at rest and during exercise. There was no mortality in this series despite the complexity of the valve insertion technique in combination with 41% concomitant procedures and the older age of our patients than of those in other studies (3–9,11). However, this echocardiographic follow-up also showed that the incidence and severity of AR increased significantly during midterm follow-up and 3 patients required reoperation for severe AR within 26 months of the primary operation.

**Homograft valve regurgitation.** Generally, most studies of cryopreserved aortic homografts report excellent results regarding freedom from reoperation due to structural valve deterioration, being 85% at 8 years (6) and 80% at 15 years (4). However, the reported incidence and severity of postoperative AR in patients with cryopreserved aortic homografts varies among different reports due to methods and length of follow-up, studied population and surgical technique (3–9,11). In previous mid- and long-term studies, AR was assessed by clinical examination (3,4), auscultation (5) or, in most recent studies, with D-E (6–9,11). AR detected by typical cardiac diastolic murmur was present in 45% of the patients with homografts at 7.5 years follow-up (5). Progressive severe AR showed with D-E was first described by Daicoff et al in a small number of young patients with freehand aortic homografts (8). Using serial D-E, which is a very sensitive method for detection and monitoring of AR, we demonstrated that also the proportion of patients with AR grade I and II increased significantly during midterm follow-up, even if the valves were perfectly competent early after the operation. Although 61% of patients developed AR grade I or II during follow-up, all of them remained clinically stable in NYHA class I or II. Patients with AR grade II were further analyzed with special regard to the left ventricular performance, but we could not demonstrate any significant change in left ventricular dimension or EF. However, the importance of mild AR for long-term results regarding valve durability and left ventricular function is still to be assessed. For that reason further long-term D-E studies seem mandatory.

Early and late outcome of homograft aortic valve replacement may be influenced by the method of implantation. When the subcoronary implantation technique is used there is a risk of malalignment of commissures or distortion of sinotubular geometry resulting in AR postoperatively. Root replacement and the inclusion cylinder techniques have been shown to reduce the incidence of postoperative AR. Dearani et al. observed a 26% risk for developing AR grade III at 7 years with the use of subcoronary technique compared to 12% risk.
when the homograft was implanted as a cylinder (11). An excellent freedom from significant AR in homografts implanted as an inclusion cylinder or as free-standing root replacement has earlier been reported by Knott-Craig et al. (25). However, similar results have been reported in a series of subcoronarily implanted homografts, with 85% freedom from AR at 8 years (6). Despite selection of patients with symmetric aortic roots and general avoidance of homograft implantation if the host annular diameter was larger than 27 mm, we found progression of AR during midterm follow-up. The experience from this study has resulted in more restrictive use of subcoronarily implanted homografts at our institution; root replacement now being the preferred technique.

**Rest and exercise hemodynamics.** The anatomy and function of the aortic annulus and coronary sinuses normally dampen the mechanical stress to which the aortic leaflets are subjected during the cardiac cycle (26). As the role of the aortic base and the central flow pattern are preserved by the use of subcoronary implantation, a better hemodynamic profile might be expected both at rest and during exercise. These expectations were fully confirmed in this study, demonstrating low maximum and mean pressure differences in all valve sizes even though 39/59 (66%) of our patients had small aortic roots and received homograft sizes ≤21 mm. During exercise with an increase in CO by 72% the ΔPmean increased only slightly, from 5.7 to 8.7 mm Hg. EOA remained unchanged during exercise for all valve sizes, suggesting that EOA is a flow-independent parameter.

The pressure differences in our study were much lower than those reported earlier for most stented bioprostheses and mechanical valves (27,28), demonstrating the excellent hemodynamic properties of aortic homografts. In the literature so far, only limited data are available regarding D-E evaluation of homograft valves (19,29,30). The only previous study dealing with exercise hemodynamics of homografts was performed with D-E 30 s after a symptom-limited supine exercise test in 27 normally functioning 20–22 mm homograft valves (30). The low pressure differences found, both at rest and after exercise, were similar to our results.

Since it is known that the short form of the modified Bernoulli equation may lead to overestimation of pressure differences at increased flow rates during exercise (27), we also used the long form of the modified Bernoulli equation, in which the velocity in LVOT is taken into consideration. However, in this study of valves with low pressure differences, the short form of the Bernoulli equation resulted in only slightly higher ΔPmax by 3.7 (1.1) mm Hg at rest and 5.1 (1.5) mm Hg at peak exercise. Similarly, for ΔPmean the mean difference between the values calculated with the short form of the Bernoulli equation, respectively, was 1.9 (0.6) mm Hg at rest and 2.7 (1.0) mm Hg at peak exercise (Table 3).

**Prosthesis-patient mismatch.** Prosthesis-patient mismatch is present when EOA of the prosthesis is less than that of the patient’s native valve and can be associated with high postoperative transvalvular pressure gradients (31). To avoid mismatch of hemodynamic importance, the valve area index should be at least 1 cm²/m² (21). Although the same criteria for homograft selection were used for all patients preoperatively and there was no indication at operation that the homograft was too small, prosthesis-patient mismatch was observed in 8 patients with different homograft sizes. We do not believe that our suture technique caused the constriction as isolated sutures were used for proximal suture line. In the present study, patients with mismatch had significantly higher pressure differences than those with valve area index ≥1 cm²/m². During exercise transvalvular velocities increased in all 31 patients, confirming that Doppler-derived pressure gradients, in contrast to what was shown for EOA, are flow-dependent (22). Our results with D-E during exercise in patients with a low valve area index suggest that the mismatch-situation accentuates this flow-dependence, with more marked increases in pressure gradients during exercise (Fig. 3). The concept of prosthesis-patient mismatch earlier described for small biological prostheses (32) but not for homografts also seems valid for homograft valves and probably accounts for higher pressure gradients in these patients. In our study, ΔPmax > 35 mm Hg during exercise was found only in patients with valve area index < 1 cm²/m² (n = 3, see Fig. 3). The midterm results regarding progression of AR or left ventricular systolic function in this study were not influenced by the mismatch situation.

**Conclusions.** Aortic valve replacement with cryopreserved subcoronarily implanted homograft can be performed safely with good clinical results. Aortic valve homograft as a valve substitute in patients with indication for a tissue prosthesis has a beneficial hemodynamic profile with low pressure differences at rest and during exercise also in patients with narrow aortic roots. Higher pressure differences were measured in the few patients with prosthesis-patient mismatch. AR grade I or II were often detected during follow-up of patients with aortic homografts. As the regurgitation progresses with time we would stress the importance of Doppler echocardiographic follow-up of these patients. In addition to studies at rest, exercise echocardiography provides further insight into valve hemodynamics, especially when prosthesis-patient mismatch is suspected.

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### References

