The Fate of Aortic Valve Homografts 12 to 17 Years After Implantation*

David J. Cohen, M.D., F.C.C.P.;† P. David Myerowitz, M.D., F.C.C.P.;‡
William P. Young, M.D.; Paramjeet S. Chopra, M.D.;
Herbert A. Berkoff, M.D.; George M. Kronke, M.D.; and
Elouise Beatty, M.S.

Results of long-term follow-up of an early cohort of patients receiving aortic valve homografts for aortic stenosis and aortic insufficiency are presented. All patients were operated upon by a single surgeon from 1966 to 1971. Eighty-three patients underwent insertion of 85 homograft aortic valves. Homografts were sterilized with either betapropiolactone (39 valves) or gamma irradiation (41 valves) and were inserted following storage in nutrient medium (16 valves) or after cryopreservation (51 valves). All homograft valves were sutured in the subcoronary position using a freehand technique. There was a 55 percent 15-year actuarial patient survival and a 16 percent 15-year actuarial homograft survival in this cohort. Homograft valve failure occurred gradually allowing the patients to be observed until they developed hemodynamic compromise at which time elective valve replacement was performed.

Because prosthetic heart valves are associated with problems of thromboembolism and because they have relatively high gradients when used in patients with a small aortic root, many surgeons have renewed their interest in the use of aortic valve homografts for valve replacement. The techniques for insertion of aortic valve homografts were independently described in 1962 by Barrett-Boyes and Ross. Homograft valves, when used in the aortic position, have a very low rate of thromboembolism without the use of anticoagulation and a low incidence of developing endocarditis. Homograft valves are ideal for use in patients with a small aortic root because a sewing ring and stent are not necessary so they have a low transvalvular gradient. With this current interest in the use of aortic valve homografts, we felt it would be instructive to review the long-term (12-17 year) outcome of aortic valve homografts in a large series of patients operated upon in a single institution.

METHODS

Eighty-three patients underwent insertion of 85 aortic valve homografts between March, 1966 and November, 1971 at the University of Wisconsin Hospital. All operations were performed by a single surgeon (W.P.Y.). Early results in 52 of these patients have been reported previously.4

Homografts were collected at post-mortem examination. Three methods of homograft preparation were utilized. Thirty-nine patients received homografts sterilized with betapropiolactone (BPL). Sixteen of these were freeze-dried. The remaining 23 of the BPL-sterilized homografts were utilized after they had been stored for one to seven days in modified Hanks' balanced salt solution. Forty-one homograft valves were utilized following sterilization with 24 megarads of gamma irradiation and storage on dry ice (−70°C) for not more than six months. All homografts were sutured in the subcoronary position utilizing the technique of Barrett-Boyes which is a free-hand, non-stented technique using continuous sutures. Anticoagulant drugs were not used unless there were indications other than valve replacement. Surviving patients were evaluated postoperatively at regular intervals. This report includes results of patient record review, questionnaires, and information from referring physicians current as of October 1985.

RESULTS

The average age of patients at the time of surgery was 45.8 years (range 14-66 years). There were 61 males and 22 females. Thirty-one of the patients were operated on for severe aortic stenosis with a mean gradient of 90 mm Hg. Twenty-four patients were operated on for severe aortic insufficiency. Twenty-eight patients had mixed aortic stenosis and insufficiency and an average aortic gradient of 72 mm Hg.

Homograft valves were prepared as noted above. There were no data obtainable on the techniques of preparation in three patients and five valves. The operative mortality in the series was 7 percent (6/83 patients). Valve survival was evaluated in relationship to the method of preparation (Table 1). There are no statistical differences in the number of valves that have been replaced or which remain in patients between groups of homografts prepared by the different techniques which were analyzed by the paired Student's t test.

Of the 40 valves that were replaced, there was no information available on nine of the valves. Of the 31

---

*From the Division of Cardiothoracic Surgery, University of Wisconsin, Madison.
†Presented at the 51st Annual Scientific Assembly, American College of Chest Physicians, New Orleans, LA, October 29, 1985.
‡Presently Associate Professor of Surgery, University of Texas Health Sciences Center, San Antonio.
§Presently Karl P. Klassen Professor and Chief, Thoracic and Cardiovascular Surgery, and Associate Professor, Department of Surgery, The Ohio State University Hospitals, Columbus.
Manuscript received July 30, revision accepted September 14.
Reprint requests: Dr. Cohen, Division of Cardiothoracic Surgery, University of Texas Health Science Center, San Antonio 78284-7941.
Table 1—Method of Preparation

|                  | BPL Fresh | BPL Dried | Irradiation
t | (−70°C) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve replaced</td>
<td>9 (39%)</td>
<td>10 (62.5%)</td>
<td>21 (51%)</td>
</tr>
<tr>
<td>Valve still in</td>
<td>2 (8.7%)</td>
<td>2 (12.5%)</td>
<td>9 (22%)</td>
</tr>
<tr>
<td>Died with valve in</td>
<td>9</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Operative death</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>16</td>
<td>41</td>
</tr>
</tbody>
</table>

valves for which there is information in the operative reports, 15 patients had calcification and/or tear and perforation of the valve leaflets, making this the most common finding. Seven patients had active or healed endocarditis. Four patients had miscellaneous leaflet abnormalities such as rolled edges, which accounted for the regurgitation. Valve leaflets looked entirely normal and pliable in three patients.

A variety of prosthetic valves were used to replace failed homografts (Table 2). The most common replacement valve used was the Bjork-Shiley prosthesis, which reflects the practice at our institution. The four patients in whom the type of valve used for replacement was unknown had their valves replaced at other institutions and these follow-up data could not be obtained.

Of the 77 operative survivors, 15 patients (19 percent) have survived a mean of 13.3 years with their homograft valve in place. There are 32 patients (41 percent) who are alive following replacement of their homograft valve. They have survived an average of 14.4 years following their original homograft valve operation. The average time elapsed from original homograft insertion to replacement of the homograft valve was 9.9 years, meaning that these patients have survived an average of 4.5 years following replacement of their aortic homograft valve.

Late mortality is reflected in the following statistics. Of the 77 operative survivors, 21 patients (27 percent) died with their homograft valve in place an average of 5.1 years following homograft valve insertion. Nine patients of the 77 operative survivors (21 percent) died following replacement of their aortic valve homograft. These patients underwent homograft valve replacement an average of six years following insertion and survived an average of 2.8 years following replacement of the homograft valve. There was only one operative death following prosthetic valve replacement of an original homograft valve—a patient managed medically at another institution who was belatedly transferred back to our institution in moribund condition for his valve replacement. Actuarial survival of patients (Fig 1) and actuarial survival of valves (Fig 2) following aortic valve homograft placement are shown. The difference in these two curves reflects the fact that a significant number of patients can be managed with an aortic valve homograft until it fails. They can then undergo replacement with a second valve and still have significantly prolonged survival.

Discussion

The use of aortic valve homografts was initially introduced and popularized at a time when the results of prosthetic aortic valve replacement were not as

Table 2—Replacement Valves

<table>
<thead>
<tr>
<th>Valve Type</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bjork-Shiley</td>
<td>21</td>
</tr>
<tr>
<td>DeBakey</td>
<td>8</td>
</tr>
<tr>
<td>Starr-Edwards</td>
<td>4</td>
</tr>
<tr>
<td>Carpentier-Edwards</td>
<td>1</td>
</tr>
<tr>
<td>St. Jude</td>
<td>1</td>
</tr>
<tr>
<td>Ionescu-Shiley</td>
<td>1</td>
</tr>
<tr>
<td>Lillehei-Kaster</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
</tr>
</tbody>
</table>

Figure 1. Actuarial survival of patients following original insertion of aortic homograft valves.

Figure 2. Actuarial survival of homograft aortic valves following initial insertion.
predictable as they are today. In fact, in comparing long-term follow-up of his series of patients in 1969, Barrett-Boyes noted survival and reoperation rates very similar to other series which utilized Starr-Edwards valves during the same era. The main differences between the homograft and prosthetic valve series were the virtual absence of emboli from a homograft valve and the fact that, unlike prosthetic valve failure, homograft valve failure from whatever cause, including cusp rupture, never resulted in sudden death. Reoperation for a failed aortic valve homograft was always possible.7

The major limitation to the use of homografts which led to abandonment of their utilization in many centers was the difficulty of procurement. Initially, homograft valves were obtained within 15 hours of death using a full sterile surgical technique. They were placed in nutrient medium and used within one to three weeks of harvest.8 These restrictions narrowly limited recipient selection because of valve availability, size restraints and logistical issues. With the introduction of betapropiolactone and later gamma irradiation for sterilization, valves could be harvested unsterile by the pathologist.9 The valves could then be kept for a longer period of time in nutrient medium. The advent of freeze-drying and lyophilization made the development of homograft valve banks possible.9 This permitted more widespread use of aortic homograft valves because of increased availability and a large variety of sizes. As seen in this study, these techniques of aortic valve homograft procurement and insertion allowed significant medium-term survival for patients with aortic stenosis and/or insufficiency.

Unfortunately, late follow-up of valves sterilized chemically or by irradiation demonstrated a significant incidence of leaflet calcification and rupture.10 This can be seen in the high late reoperative rate of our own series. This late homograft deterioration is probably because such valves are nonviable. Antibiotic sterilization was used by Barrett-Boyes and associates11 beginning in 1968 and low-dose antibiotic sterilization was introduced in 1969 by O’Brien et al.12 Their valves were implanted either fresh after storage in nutrient medium or following cryopreservation using techniques developed by Mermet, Buch and Angell13 in the early 1970s. These improved techniques have allowed up to 92 percent freedom from reoperation at ten years in the low-dose antibiotic-treated, cryopreserved group.10 A debate rages as to whether these improved results are due to valve viability as a result of less toxic doses of antibiotics and improved cryopreservation techniques.10,13-14

This long-term follow-up study of an early series of patients undergoing aortic valve replacement with homograft valves demonstrates significant medium and long-term survival even using these older techniques of valve procurement and preservation. There was no difference in valve durability in this series between the types of preservation and sterilization techniques used. Newer techniques of valve sterilization using low-dose antibiotics and better methods of cryopreservation, however, mandate a renewed consideration of the aortic valve homograft for patients with small aortic roots, in patients with contraindications to anticoagulation, and probably in patients with bacterial endocarditis.

Finally, this study demonstrates that homograft valve failure occurs gradually. These patients may be followed until they develop signs and symptoms of hemodynamic compromise, and a murmur of aortic insufficiency is probably not, in itself, an indication for replacement of the homograft valve.

REFERENCES
8 Phelan J, Young WP, Schmidt ER. Recent developments in the sterilization of arterial homografts. Wis Med J 1958; 57:239-40
9 Phelan JT, Young WP, Botham RJ, Gale JW, Schmidt ER. The development of the artery bank at the University Hospitals. Wis Med J 1958; 57:232-34

484 Fate of Aortic Valve Homografts (Cohen et al)