Homograft Replacement of the Mitral Valve

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SUMMARY

Replacement of the mitral valve with an aortic valve homograft has become feasible. Clinical and hemodynamic assessments of eight patients who received the new homograft were made from 3 to 6 months following surgery. Marked improvement was reported by six patients and mild to moderate improvement by two. At rest the homografts functioned well, creating a trivial diastolic gradient between the left atrium and left ventricle and being mildly insufficient in two cases. On exercise there was moderate mitral insufficiency. Anticoagulants were used for 3 months following surgery and then discontinued. In 60 subsequent patient-months no thromboembolism has been observed. The data are as yet inconclusive, but the homograft shows promise of being a reasonable alternative to the prostheses currently in use.

Additional Indexing Words:
Aortic valve homograft  Hemodynamic assessment  Anticoagulants
Thromboembolism

During the past 6 years orthotopic homografts have been used widely to replace diseased aortic valves, and the clinical results have been comparable to those obtained with prosthetic valves.\(^1\)\(^-\)\(^3\) Scattered reports describing the use of homografts as substitutes for mitral valves have appeared,\(^4\)\(^-\)\(^6\) but prosthetic valves continue to be the standard replacements for diseased mitral valves. The prosthetic valves have several shortcomings. They produce a small diastolic pressure gradient between the left atrium and left ventricle in resting patients and a substantial gradient during exercise.\(^7\) Their mass is such that they sometimes interfere with left ventricular function.\(^8\) Finally, they represent foreign bodies which can initiate thrombus formation, and despite the standard use of anticoagulants, peripheral embolization frequently occurs.\(^9\)\(^,\)\(^10\)

For these reasons, aortic valve homografts have recently been adapted so that they can be substituted for diseased mitral valves. The anticipated advantages of the homograft valve are that it will not necessitate the chronic use of anticoagulants and since it is not as bulky as the prosthesis, the danger of interference with left ventricular function will be reduced. Furthermore, the orifice area of the homograft is greater than that of the prosthetic valve. Accordingly, obstruction to flow across the mitral valve should be lessened.

The subject of this study is an assessment of homograft replacement of the mitral valve. Clinical and hemodynamic evaluations were made before and after mitral valve replacement and are reported.

Methods

Eight patients were studied. The only factor involved in selection for study was the requirement that the patients survive for at least 3 months following surgery. The eight who were evaluated were among the first 15 who underwent surgery. To date homograft replacement of
**Table 1**

**Preoperative Hemodynamic Data**

<table>
<thead>
<tr>
<th>Patient</th>
<th>L.O.</th>
<th>M.B.</th>
<th>E.B.</th>
<th>A.P.</th>
<th>D.D.</th>
<th>R.C.</th>
<th>K.B.</th>
<th>V.B.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex &amp; age (yr)</td>
<td>F-32</td>
<td>M-47</td>
<td>M-38</td>
<td>F-49</td>
<td>F-35</td>
<td>M-66</td>
<td>F-55</td>
<td>F-42</td>
</tr>
<tr>
<td>Lesion (s)</td>
<td>MS, AS, TS</td>
<td>MI, AS</td>
<td>MS, AS</td>
<td>MS, TI</td>
<td>MI, MS</td>
<td>MI</td>
<td>MI, MS</td>
<td>MI, MS</td>
</tr>
<tr>
<td>Rhythm</td>
<td>A-V diss.</td>
<td>NSR</td>
<td>AF</td>
<td>AF</td>
<td>AF</td>
<td>AF</td>
<td>AF</td>
<td>AF</td>
</tr>
</tbody>
</table>

**Rest**

**Pressures (mm Hg)**
- PA (s/d/m) |
  - 53/29/40
  - 44/23/30
  - 38/14/22
  - 50/37/37
  - 52/20/35
  - 54/23/32
  - 35/16/23
- PAW (a/v/m) |
  - 29/38/30
  - 34/35/31
  - 21/17
  - 35/25
  - 35/20
  - 40/24
  - 33/20
- LA (a/v/m) |
  - 34/44/37
  - 34/34/37
  - 21/15
  - -
  - -
  - -
  - -
- LV (s/ed) |
  - 190/34
  - 121/7
  - 115/11
  - -
  - -
  - -
  - -

**Cardiac index**
- (L/min/m²) |
  - 1.7
  - 2.5
  - 4.0
  - 1.9
  - 2.2
  - 2.1
  - 2.1
  - 1.3

**Arteriovenous O₂ diff.**
- 8.5
- 5.2
- 4.2
- 6.8
- 6.0
- 6.5
- 6.1
- 8.5

**Exercise**

**Pressures (mm Hg)**
- PA (s/d/m) |
  - 67/37/32
  - 84/32/50
  - 83/54/64
  - 63/36/50
  - -
  - 60/35/43
- PAW (a/v/m) |
  - -
  - -
  - -
  - -
  - -
  - -
- LA (a/v/m) |
  - -
  - -
  - -
  - -
  - -
  - -
- LV (s/ed) |
  - 230/65
  - -
  - -
  - -
  - -
  - -

**Cardiac index**
- (L/min/m²) |
  - 4.3
  - 3.5
  - 3.5
  - 2.7
  - 2.5
  - 2.7
  - 2.2

**Arteriovenous O₂ diff.**
- 11.4
- 13.0
- 10.7
- 10.7
- 11.1
- 11.9
- 14.4

Abbreviations: MS = mitral stenosis; AS = aortic stenosis; TS = tricuspid stenosis; TI = tricuspid insufficiency; MI = mitral insufficiency; PA = pulmonary artery; PAW = pulmonary artery wedge; LA = left atrium; LV = left ventricle; a = a wave; v = v wave; m = mean; s = systolic; d = diastolic; ed = end-diastolic; A-V diss. = A-V dissociation; NSR = normal sinus rhythm; AF = atrial fibrillation.
The mitral valve homograft is pictured in two views: (A) In profile, with atrial aspect downward. (B) With leaflets apart, from ventricular aspect.

The mitral valve homograft was secured to a Teflon-covered titanium strut, with an internal diameter of 27, 28, or 29 mm (fig. 1). The technique of insertion of the homograft valve into the mitral annulus of the patient was similar to that employed for the prosthetic valve.

Postoperative Assessment

All patients were hospitalized between 3 and 6 months following surgery for right and left heart catheterization. Six reported marked improvement, and the other two, moderate improvement. According to the New York Heart Association Classification, seven fell into functional class II and one in class III. Roentgenograms of five patients showed reduction in the left atrial and the overall cardiac size. There was either no change or a slight increase in cardiac size in three patients.

The results of postoperative cardiac catheterization are summarized in table 2. Mean left atrial postoperative pressure at rest was 13 mm Hg or less in seven patients, and 20 mm Hg in the eighth. The average reduction in mean left atrial pressure from preoperative level was 12 mm Hg (48%) (fig. 2A). Mean pulmonary artery pressure also fell, the average decrease being 7 mm Hg (23%) (fig. 2B). In five patients simultaneous measurements were made of left ventricular and left atrial or pulmonary artery wedge pressure. The mean diastolic pressure gradient

Preparation of Homografts and Technique of Surgery

Under sterile conditions the aortic valve was removed from a cadaver within 10 hours of death. The valve was stored at 4 C in a nutrient medium (TC 199*) with 10,000 units of penicillin and 10,000 µg of streptomycin per milliliter. Each valve was cultured to assure sterility before use in patients. Immediately before use, the

* Tissue Culture 199, Grand Island Biological, Grand Island, New York.
Changes following surgery (at rest) in mean left atrial pressure (A), mean pulmonary pressure (B), and cardiac index (C). Preoperative values are at the left of each panel, and postoperative values at the right. Left atrial and pulmonary artery pressures decreased after surgery, and cardiac index increased (see text). Where direct left atrial pressure was not measured pulmonary artery wedge pressure was assumed to be equal to left atrial pressure.

Across the mitral valve at rest for the entire group was 2.7 mm Hg, and diastasis was achieved in six cases (fig. 3). In two patients there was evidence of mild to moderate mitral insufficiency at rest, on the basis of left atrial v waves of 26 and 31 mm Hg (fig. 4). Six of the eight patients underwent left ventriculography. In four cases there was no or
### Table 2

**Postoperative Hemodynamic Data**

<table>
<thead>
<tr>
<th>Valve(s) replaced</th>
<th>Patient</th>
<th>L.O.</th>
<th>M.B.</th>
<th>E.B.</th>
<th>A.P.</th>
<th>D.D.</th>
<th>R.C.</th>
<th>K.B.</th>
<th>V.B.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>M, T, A</td>
<td>M, A</td>
<td>M, A</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td><strong>Pressures (mm Hg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA (s/d/m)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>31/13/20</td>
<td>43/21/30</td>
<td>25/11/16</td>
<td>56/27/32</td>
<td>50/19/26</td>
<td>25/13/18</td>
</tr>
<tr>
<td>PAW (a/v/m)</td>
<td>-</td>
<td>-</td>
<td>-/16/13</td>
<td>-/15/11</td>
<td>-/11/8</td>
<td>-/30/21</td>
<td>-</td>
<td>-/13/9</td>
<td>-/15/9</td>
</tr>
<tr>
<td>LA (a/v/m)</td>
<td>14/7/8</td>
<td>15/26/13</td>
<td>-</td>
<td>-/15/12</td>
<td>-/10/6</td>
<td>-/31/20</td>
<td>-/13/9</td>
<td>-/15/10</td>
<td></td>
</tr>
<tr>
<td>LV (s/ed)</td>
<td>91/7</td>
<td>115/13</td>
<td>148/5</td>
<td>110/12</td>
<td>136/2</td>
<td>145/14</td>
<td>134/13</td>
<td>120/6</td>
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<tr>
<td><strong>Mean diast. gradient LA-LV</strong></td>
<td>0.5</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td></td>
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<tr>
<td><strong>Cardiac index</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(L/min/m²)</td>
<td>3.2</td>
<td>3.0</td>
<td>3.7</td>
<td>2.4</td>
<td>2.6</td>
<td>2.8</td>
<td>2.4</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td><strong>Arteriovenous O₂ diff.</strong></td>
<td>4.6</td>
<td>4.5</td>
<td>4.2</td>
<td>6.3</td>
<td>5.4</td>
<td>5.4</td>
<td>4.6</td>
<td>5.9</td>
<td></td>
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<tr>
<td><strong>Heart rate</strong></td>
<td>78</td>
<td>78</td>
<td>88</td>
<td>84</td>
<td>90</td>
<td>114</td>
<td>60</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td><strong>Exercise</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Pressures (mm Hg)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>PA (s/d/m)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>48/18/33</td>
<td>57/29/40</td>
<td>-</td>
<td>75/38/53</td>
<td>-</td>
<td>50/17/28</td>
</tr>
<tr>
<td>PAW (a/v/m)</td>
<td>-</td>
<td>-</td>
<td>-/26/21</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>LA (a/v/m)</td>
<td>-</td>
<td>23/55/32</td>
<td>-</td>
<td>-/35/23</td>
<td>-/35/26</td>
<td>-/54/30</td>
<td>-/34/25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV (s/ed)</td>
<td>-</td>
<td>150/22</td>
<td>140/16</td>
<td>145/6</td>
<td>162/3</td>
<td>153/15</td>
<td>176/19</td>
<td>-/15</td>
<td></td>
</tr>
<tr>
<td><strong>Mean diast. gradient LA-LV</strong></td>
<td>-</td>
<td>7</td>
<td>9</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac index</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(L/min/m²)</td>
<td>-</td>
<td>3.9</td>
<td>4.8</td>
<td>2.6</td>
<td>3.3</td>
<td>2.7</td>
<td>3.6</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td><strong>Arteriovenous O₂ diff.</strong></td>
<td>-</td>
<td>10.2</td>
<td>8.4</td>
<td>10.7</td>
<td>10.0</td>
<td>12.4</td>
<td>8.5</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td><strong>Heart rate</strong></td>
<td>-</td>
<td>102</td>
<td>116</td>
<td>102</td>
<td>108</td>
<td>150</td>
<td>90</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td><strong>LV cine</strong></td>
<td>No MI</td>
<td>Mod MI</td>
<td>No MI</td>
<td>No MI</td>
<td>No MI</td>
<td>No MI</td>
<td>Mild MI</td>
<td>Min MI</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: M = mitral; T = tricuspid; A = aortic; a = a wave; v = v wave; m = mean; s = systolic; d = diastolic; ed = end-diastolic; PA = pulmonary artery; PAW = pulmonary artery wedge; LA = left atrium; LV = left ventricle; mod = moderate; min = minimal; MI = mitral insufficiency; LV cine = left ventricular cineangiography.
minimal mitral insufficiency, and in two there was mild to moderate insufficiency. Five patients had the left atrial pressure measured during exercise. Mean left atrial pressure rose considerably, the average increase being 14 mm Hg. The mean left atrial v wave was 40 mm Hg and the average of the mean left atrial pressures, 26 mm Hg. During exercise the mean diastolic gradient across the mitral valve was 7 mm Hg. Three patients (I.O., M.B., and E.B.) also had orthotopic aortic valve homografts which were functioning well without gradients or evidence of insufficiency. One of the three had, in addition, an aortic valve homograft in the tricuspid position (I.O.), and the graft's function was normal. Finally, one patient (A.P.) had evidence of organic tricuspid insufficiency and mild aortic stenosis.

The changes in mean left atrial pressure, mean pulmonary artery pressure, and cardiac index resulting from surgery in the three patients mentioned above (I.O., M.B., and E.B.) reflected, in part, replacement of their aortic (and tricuspid) valves. In order to isolate the effect of mitral valve replacement, it is necessary to focus on the five patients in whom mitral replacement alone was performed. The hemodynamic changes observed in these five were similar to those occurring in the group as a whole. The average of their mean left atrial pressures fell from 21 to 12 mm Hg (−43%). The change in mean pulmonary artery pressure was from 30 to 24 mm Hg (−20%), and the average cardiac index rose from 1.9 to 2.5 L/min/m² (+31%). The corresponding values for the group as a whole were −48%, −23%, and +27%. It is clear, then, that homograft replacement of the mitral valve alone produced considerable hemodynamic improvement.

On exercise, however, the A-V oxygen difference increased excessively—to 10.4 vol% for the entire group and to 10.8 vol% for those who underwent mitral replacement alone. The rise in cardiac output was small—to 3.3 L/min/m² for the entire group and to 2.9 L/min/m² for the five whose mitral valves alone were replaced. The poor response to exercise in terms of cardiac output was probably due, at least in part, to the fact that moderately severe mitral insufficiency developed. In addition, one patient (A.P.) had significant residual tricuspid insufficiency.

All patients were treated with anticoagulants following surgery. Administration of anticoagulants was discontinued approximately 3 months after surgery, and in 60 patient-months of follow-up no thromboembolic phenomena have been observed.

**Discussion**

The hemodynamic data detailed in this study indicate that the new homograft valve functions well in humans as a replacement for the diseased mitral valve. Patients receiving the homografts were greatly benefited clinically. Their resting left atrial and pulmonary artery pressures fell considerably, while their cardiac outputs rose. During exercise mild to moderate insufficiency of the homograft developed, as manifested by left atrial v waves of 34 to 55 mm Hg. In a study of the pathology of human aortic valve homografts, Smith reported that the grafts were consistently enveloped by fibrous sheaths (neo-intima) which developed from adjacent host tissue. The host cellular response consisted of mild chronic inflammation with infiltration of neo-intima by granulation.

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*Figure 3*

*Simultaneous left atrial and left ventricular pressures from one patient (D.D.) showing equilibration of pressures throughout diastole.*
tissue. Similar changes may well have been responsible for the mitral insufficiency observed in our patients.

The immediate basis for use of the homograft under investigation rests on dog experiments, the results of which are to be reported. The canine homografts functioned well for as long as 6 months, and the dogs were sacrificed, so that the homografts could be examined. Mild mitral insufficiency associated with shortening and thickening of the valve leaflets tended to develop in the animals after several months.

Smith's findings and those of others indicate that neo-intima develops on the homograft within several months. Therefore, the patients in this series were treated with anticoagulants for 3 months following surgery. With the formation of neo-intima, no thrombogenic surface remains in the bloodstream and the necessity for anticoagulants is removed.

When replacement of the mitral valve is necessary, the current standard practice is to use a prosthetic valve. A comparison, then, of a representative prosthesis with the new

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**Figure 4**

Left atrial pressure from one patient (M.B.) showing prominent v wave (26 mm Hg) suggesting mitral insufficiency. The simultaneous ventricular end-diastolic pressure was 13 mm Hg.
HOMOGRaFT MITRAL VALVE REPLACEMENT

homograft is in order. Morrow and associates showed that the Starr-Edwards prosthetic valve causes a mean diastolic gradient between the left atrium and left ventricle of 5 to 6 mm Hg and that the gradient rises to 9 mm Hg on exercise. The corresponding gradients produced by the homograft are 2.7 and 7 mm Hg. Furthermore, none of the Starr-Edwards valves studied allowed equilibration of atrial and ventricular pressures throughout diastole, whereas two of the homografts did (fig. 4). These data reflect the fact that the orifice area of the homograft is larger than that of the prosthetic valve. On the other hand, patients with homograft valves developed striking v waves (mean, 40 mm Hg) on exercise, indicating that the valves had become moderately insufficient. The average of the mean left atrial pressures rose to 25 mm Hg during exercise, reflecting the mitral insufficiency or some degree of myocardial failure, or both. By comparison, the mitral prostheses studied by Morrow and associates were associated with mean left atrial pressures (on exercise) averaging 19 mm Hg. In summary, it appears that the homograft causes less obstruction to ventricular filling, both at rest and on exercise, than does the prosthesis. However, the homograft tends to be insufficient, minimally at rest and moderately on exercise.

Since the ring and struts supporting the homograft are considerably smaller than the cage of the prosthetic valve, the likelihood of interference with left ventricular function is less when the homograft is used. Furthermore, the initial results suggest that the homograft will not predispose to thromboembolism to the same extent as the prosthesis.

The Starr-Edwards prosthesis, however, has recently been altered with the purpose of reducing or eliminating the incidence of thromboembolism. Teflon cloth formerly covered only a portion of the base of the prosthesis. Teflon now covers the entire base of the prosthesis, so that the only exposed metal consists of the cage legs and the ball seat. Preliminary data seem to indicate that the incidence of thromboembolism has been reduced. 14

References
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Circulation. 1968;38:664-671
doi: 10.1161/01.CIR.38.4.664
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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