CURRENT TOPICS

THE PROBLEM OF VALVE PROSTHESIS-PATIENT MISMATCH

SHAHBUDIN H. RAHIMTOOLA, M.D.

SUMMARY Valve prostheses have played an important part in the past two decades in the management of patients with valvular heart disease. However, many of the devices used in valve replacement have introduced new clinical problems. This paper deals with some of the problems associated with valve replacement, including one not previously emphasized — valve prosthesis-patient mismatch, which may cause obstruction to ventricular outflow and/or inflow.

VALVE REPLACEMENT has been the most important advance in the last 19 years in the management of patients with valvular heart disease.1 If valve replacement is successful and uncomplicated, many patients experience an improvement in the symptomatic state2 21 and, therefore, in the quality of life. Following mitral valve surgery pulmonary hypertension is relieved,22-25 and following aortic valve replacement the compensatory mechanisms of hypertrophy and/or ventricular dilatation regress,26 27 and impaired ventricular performance improves.5 27 However, the devices used for valve replacement have not been perfect; they have introduced other, new problems into clinical medicine, so that in effect, the patient is exchanging one disease process for another. Many complications associated with valve replacement continue to receive widespread attention, such as thromboembolism, bleeding from anticoagulant therapy, valve dysfunction and valve re-replacement.1 21 28-37

Another problem with valve replacement devices is valve prosthesis-patient mismatch. This problem has not received much emphasis and should be considered before the indications for valve replacement are broadened.39 Mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve. The reduced prosthetic valve area is usually mild to moderate in severity and often of no immediate clinical significance. However, occasionally it can be a severe problem because the patient may be hemodynamically and symptomatically worse after valve replacement (table 1); other patients with bioprosthetic mitral and aortic effective valve areas of \( \leq 1.0 \text{ cm}^2 \) have also been reported from other centers.11-18 The mismatch results mainly from two factors. First, the in vivo effective prosthetic valve area of almost all types of valve replacement devices that can be inserted in most patients is less than that of the normal human valve. The in vivo effective prosthetic valve area is even further reduced because of tissue ingrowth and endothelialization, and therefore, these devices can be considered “stenotic.” Second, in some patients the problem is compounded because the size of the prosthesis that can be inserted is limited by the size of the annulus, which is small compared to the size of the patient, and also by the size of the cavity in which the prosthesis must lie.

The normal aortic valve area is 3-4 cm² or greater and the normal mitral valve area is 4-5 cm²,30 areas rarely approached with prosthetic valves. Valve replacement devices are basically of the mechanical or biological varieties. Of the mechanical prostheses, the ones most commonly used in this country are the ball and cage and the tilting disc valves. Of the biological devices, the porcine heterograft is most commonly used in the United States, where the use of homografts has declined because of the problem of late valve failure.30 However, it is still being used in New Zealand and in Europe.17-19 Other xenografts, made of pericardium and of dura mater, are in use in Europe and in South America.20, 21 The porcine heterograft is smaller than the normal human valve because the pig is smaller than adult man; and the xenograft is mounted on metallic rings, which makes it a bioprosthesis and further reduces the effective orifice size. The problem is exacerbated by certain characteristics of the pig aortic valve. All prostheses (mechanical and bioprostheses) have an in vitro effective orifice area that is smaller than that of the normal human valve. For example, most prosthetic valves that can be inserted in the aortic position have an in vitro effective orifice areas of less than 3 cm²; usually they are less than 2.5 cm². In addition, after valve insertion there is tissue ingrowth and endothelialization which reduces the in vivo effective prosthetic valve area to less than the in vitro valve area,2 4, 8-15, 36, 40, 41 and therefore, all valve replacement devices can be considered to be “stenotic,” even if they are “normal.”

An appreciation of this problem is obtained by examining valve areas in a group of patients who have undergone prosthetic valve replacement for isolated severe aortic incompetence. These patients had no systolic outflow gradients preoperatively and their aortic valve rings were large, which allowed a large valve replacement device to be inserted. Figure 1 shows that in these patients the calculated valve area of ball and cage prostheses averaged 1.7 cm², valve areas that have usually been considered to be satisfactory and to indicate normal prosthetic function.5 40 41
TABLE 1. Male, 58 years old, had a ball and cage prosthesis in 1967 for mitral valve disease. Largely because of repeated systemic emboli the competent mechanical prosthesis was changed to a bioprosthesis in February 1976. Following valve re-replacement patient deteriorated symptomatically and the calculated bioprothetic valve area was smaller than present prior to valve re-replacement.

<table>
<thead>
<tr>
<th></th>
<th>Prior to valve re-replacement</th>
<th>After valve re-replacement</th>
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</thead>
<tbody>
<tr>
<td>Brachial artery (mm Hg)</td>
<td>8/26/75</td>
<td>11/5/76</td>
</tr>
<tr>
<td>Left atrium or pulmonary artery wedge (mm Hg)</td>
<td>V = 25 (16)</td>
<td>V = 46 (37)</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>32/20 (25)</td>
<td>76/40 (52)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Mean mitral gradient (mm Hg)</td>
<td>12</td>
<td>22</td>
</tr>
<tr>
<td>Mitral valve area (cm²)</td>
<td>1.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Mitral valve area index (cm²/m²)</td>
<td>0.89</td>
<td>0.54</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Ventricular rate (per min)</td>
<td>80</td>
<td>96</td>
</tr>
</tbody>
</table>

However, these valve areas relate to patients of different sizes; correcting these for body surface area demonstrates that the average prosthetic aortic valve area in these patients was only 1 cm²/m², with a range of 0.7–1.6 cm²/m². If one recalls that, in the unoperated state, severe aortic valve stenosis is considered to be present when the aortic valve area index is ≤ 0.75 cm²/m²,42,43 or is ≤ 0.60 cm²/m²,44 (≤ 1.0 cm²)45 then it is clear that the valve abnormality in many of these patients has, in fact, been converted from severe aortic regurgitation to mild to moderate left ventricular outflow obstruction. In general, the tilting disc prostheses6,9,34 and the bioprostheses11–13,36 have similar average effective orifice sizes, and thus, are not free of the problem.

Effective orifice size is only one factor that has to be taken into account when selecting a valve replacement device for an individual patient. In the smaller valves the tilting disc prostheses have a larger effective orifice size than the bioprostheses and the ball and cage valves.3,8–15,40,41,46,47 On the other hand, patients with bioprostheses11–13,17–21 do not appear to be in need of anticoagulant therapy, which is usually essential in patients with all types of mechanical prostheses1,2,8–10,28–35 and the ball and cage prosthesis has a proven durability of at least 15 years,22 while patients with other valve replacement devices have not been followed for such a long time;23–21 and therefore, the long-term durability of the other devices is unknown.

In patients with valvular stenoses, the annulus into which the prosthesis has to be inserted is usually smaller than that present in valvular incompetence. As a result, the prosthetic valve areas tend to be smaller in patients who have undergone valve replacement for a stenotic valve. For example, in a select group of patients we have reported,27 the prosthetic valve areas were 29% smaller in patients undergoing valve replacement for aortic stenosis than in those undergoing valve replacement for aortic incompetence (1.25 cm² vs 1.76 cm²). When the annulus is quite small, following valve replacement many patients may be left with obstruction to left ventricular outflow and/or inflow that is moderate to severe; this occurs both with

Figure 1. The valve areas (open circles) of a ball and cage prosthesis, when corrected for body size (closed circles), afford a better knowledge of the hemodynamic consequences of the device in a particular patient. For example, in two patients the calculated prosthetic valve areas were identical (2.1 cm²). Since the patients were of different sizes, the prosthetic valve areas, corrected for body size in the two patients, were quite different (1.1 and 1.6 cm²/m²).
the mechanical and the bioprostheses. As a result, when valve replacement is undertaken for valve stenosis that is moderate rather than severe, the patient may have a postoperative hemodynamic state that is the same as the preoperative state (table 2). To overcome the problems of a very small annulus, newer surgical techniques have been directed to enlarging the annulus, which would permit the implantation of a larger prosthesis, and the use of valved left ventricular apical-aortic conduits for relief of left ventricular outflow obstruction. The long-term benefits of these techniques have not yet been proven.

It may be questioned that if valve replacement devices are inherently "stenotic" and most patients are left with mild to moderate obstruction, then why: 1) do a few patients have no gradient across the prostheses? 2) are many patients symptomatically improved? 3) do compensatory mechanisms often regress? and 4) may ventricular performance be improved? The answers become apparent when one examines the relationship of gradient to valve area (fig. 2). Usually, no outflow gradient can be demonstrated across narrowed aortic valves until the effective orifice size is reduced to less than 40–60% of the normal valve area. A similar phenomenon also occurs with stenosed arteries. Therefore, it is possible to have a stenotic valve and have no demonstrable gradient. 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. As a result, small increases in valve area of critically narrowed valves will result in large and major reductions of gradient. Thus, it is possible to increase valve area from the severe to the mild to moderate range and bring about a major reduction in gradient. When this occurs in aortic stenosis, there is a major reduction in afterload on the left ventricle and as a result ventricular hypertrophy will regress and ventricular performance will improve, if it was impaired preoperatively.

A similar phenomenon occurs with mitral stenosis. In the mid-1950s, when closed mitral commissurotomy was performed through the atrium for critical mitral stenosis, the patient was often left with moderate mitral stenosis. However, since the gradient was reduced to a major degree, mean left atrial pressure fell to less than pulmonary edema levels and the patient obtained dramatic relief of the symptoms of mitral stenosis even though he continued to have

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**TABLE 2.** Male, 37 years old, had a ball and cage prosthesis in 1969 for mitral valve disease. He had repeated episodes of atrial tachycardia that repeatedly put him into pulmonary edema. Prophylaxis for atrial tachycardia was not very successful. He underwent re-replacement of the complete mechanical prosthesis with a bioprosthesis in order to obtain a larger effective orifice size which would have reduced the frequency and severity of pulmonary edema with atrial tachycardia. Following valve re-replacement the patient's condition was unchanged.

<table>
<thead>
<tr>
<th>Prior to valve re-replacement</th>
<th>After valve re-replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
</tr>
<tr>
<td>7/14/76</td>
<td></td>
</tr>
<tr>
<td>Brachial artery (mm Hg)</td>
<td>132/60</td>
</tr>
<tr>
<td>Left ventricle (mm Hg)</td>
<td>130/11</td>
</tr>
<tr>
<td>Left atrium (mm Hg)</td>
<td>A20</td>
</tr>
<tr>
<td>Pulmonary artery (mm Hg)</td>
<td>V20 (14)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.1</td>
</tr>
<tr>
<td>Mean mitral gradient (mm Hg)</td>
<td>8</td>
</tr>
<tr>
<td>Mitral valve area (cm²)</td>
<td>1.5</td>
</tr>
<tr>
<td>Mitral valve area index (cm²/m²)</td>
<td>0.75</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>yes</td>
</tr>
<tr>
<td>Heart rate (per min)</td>
<td>55</td>
</tr>
</tbody>
</table>

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**FIGURE 2.** Diagrammatic representation of the relationship of mean systolic gradient to the aortic valve area, assuming the cardiac output and velocity of flow are constant. The curve is based upon knowledge of the hydraulics of a stenotic valve and of experimental data. The approximate zone of prosthetic valve area to gradient is based on published data.
moderate mitral stenosis. This phenomenon is still seen. Thus, symptomatic improvement does not mean that the effective prosthetic orifice area is optimum. Moreover, the long-term effects of the prosthetic stenotic lesions have not been fully studied, and it is possible that this may account for the unexplained lack of improvement seen in some patients and for unexplained late complications, such as late deterioration of cardiac function.

sudden prosthetic thrombosis and sudden death.

Clinical Implications

The reduced effective orifice size of valve prostheses has usually been referred to euphemistically as a problem of gradients. It should be recognized for what it really is — obstruction to ventricular outflow and/or inflow. Usually, the obstruction is of mild to moderate severity, but at times, it is moderate to severe. This has several important clinical applications:

1) An effective prosthetic valve area that may be acceptable for a small, inactive, patient is usually unsatisfactory for a larger, physically active individual. Therefore: a) the calculated absolute effective orifice size (cm²) which gives an idea of the function of the prosthetic valve has to be corrected for body size (cm²/m²) to better understand the hemodynamic and functional implications of the device for an individual patient; and, b) the function of the device needs to be studied not only at rest but also at a different hemodynamic state, such as exercise, because hemodynamic measurements made in the resting supine patients are not necessarily representative of the patient’s usual hemodynamic state.

2) Some patients, because of a small annulus and/or tissue ingrowth and thrombus, will be left with effective prosthetic valve areas that are in the moderate to severe stenotic range. In such patients, a small amount of additional tissue ingrowth or thrombus may produce critical stenosis which at times may occur suddenly, and thus, these patients are at risk of relatively acute and sudden deterioration in cardiac function. This may account for some instances of sudden prosthetic thrombosis and sudden death.

3) Before recommending valve replacement in patients with borderline indication for valve replacement, the cardiologist and cardiac surgeon must attempt to project the postoperative result considering the patient’s hemodynamic state and the performance of the prosthesis that will be inserted.

4) When evaluating the late results of valve replacement (for example, on survival, on functional class and on left ventricular function), the poor late results in some patients may be the result of the delayed effects of moderate to severe prosthetic stenosis. Therefore, it is important to evaluate prosthetic function accurately before ascribing undesirable late results to causes other than the prosthesis.

To solve the problem, it is important that the search for better valve replacement devices is continued until the perfect or ideal device is found. Meanwhile, there is also a need for a technique which will permit accurate preoperative prediction of the valve size the surgeon will realistically be able to insert in an individual patient, keeping in mind that even large size prostheses may be undesirably stenotic in large individuals.

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