Multiple Valve Replacement
Review of Five Years' Experience

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SUMMARY
During the past 5 years 152 patients have undergone multiple valve replacement
in this clinic. The operative mortality is 12% and the late mortality 14%. The late
complications and functional results of the 112 survivors are reviewed and discussed.
Neither severe cardiovascular symptoms nor unfavorable hemodynamic findings are
specific contraindications to an operation; however, irreversible disease coexisting
in other organ systems is a possible contraindication. A decrease in recent operative
mortality and fewer significant complications suggest that this experience should be extended.

Additional Indexing Words:
Valve replacement   Prosthetic heart valves   Multiple valve disease

The MANAGEMENT of patients whose
advanced valvular heart disease requires
the replacement of more than one valve has
improved greatly during the past 5 years. The
most significant changes have been the de-
velopment of more suitable prostheses, a more
complete diagnosis of associated pathological
valves, and an improved aggressive operative
approach. It is now possible to operate upon
these patients with a risk nearly identical to
isolated valve disease patients. This report
reviews 152 patients who have undergone
multiple valve replacement at the University
of Oregon Medical School between June 1962
and January 1968.

Clinical Material
There were 152 patients in this series. Aortic
and mitral valve replacement was performed in
103, mitral and tricuspid replacement in 16,
and aortic, mitral, and tricuspid replacement in
33. Two patients with previous aortic valve re-
placement subsequently had a mitral valve re-
placement. One patient with an isolated mitral
valve replacement subsequently had an aortic
valve implanted, and three subsequently had a
tricuspid valve implanted.

The age distribution of the patients is indicated
in figure 1, with a range from 20 to 66 years
and a mean of 47 years. An additional 31
patients have undergone isolated valve replace-
ment and concomitant valvulotomy or valvu-
loplasty of one or more of the remaining valves.
They are not included in the above total. Fifteen
per cent of the patients had previously closed
mitral commissurotomy.

All patients selected for operation were func-
tional class III or IV by the New York Heart
Association Classification System. Their clinical
appearance was dominated by the symptoms and
physical signs of either long-standing mitral or
aortic valve disease. Most of the patients had
complete cardiac catheterization, and supravalvu-
lar and left ventricular angiograms. Many had
selective coronary angiography in addition. A
final accurate diagnosis can only be made during
surgical exploration of the pathologic anatomy.

No patient has been denied surgery because of
the severity of cardiac disability as determined
either clinically or by hemodynamic studies.
Surgery has been denied to some patients with
serious associated disease such as alcoholic
cirrhosis, chronic renal failure, and pulmonary
fibrosis and emphysema. Ten patients beyond
the age of 60 have undergone multiple valve
replacement and nine are surviving. It does not
MULTIPLE VALVE REPLACEMENT

AGE DISTRIBUTION

June 1962 - Jan. 1968 152 Patients

Operative Deaths

2 12 25 55 49 9
10-20 21-30 31-40 41-50 51-60 61-70

Figure 1

The age distribution of 152 patients undergoing multiple valve replacement and the operative mortality for the age groups are shown graphically.

appear that age alone contraindicates an operation.

Patients are admitted to the hospital at least 1 week prior to operation to gain the maximum benefit of medical therapy. This allows the patient’s staphylococcal flora to be controlled and any occult foci of infection to be identified and treated. Dental examination is an important part of the initial workup, and abscessed teeth should be treated prior to the operation. Cultures of the urine and external nares are obtained. The patients undergo a rigid program of antibiotic prophylaxis with instillation of a broad-spectrum antibiotic ointment into the nasal vestibule, showers or bed baths with surgical soap twice daily, and a shampoo every other day. Parenteral penicillin, methicillin and streptomycin are given the day before operation and for 1 week postoperatively. Penicillin-sensitive patients are treated with cephalothin. Long-acting digitalis preparations are withheld 24 to 48 hours prior to operation. Fluid restriction is employed if a rapid weight gain occurs during the preoperative period; diuretics are withheld except in patients with overwhelming congestive heart failure. Occasionally peritoneal dialysis is required to reverse the failure. Many of these patients are receiving an anticoagulant at the time of admission. The drug is discontinued early enough to assure normal prothrombin function. In the presence of congestive hepatomegaly this may require 5 to 6 days and supplemental vitamin K. Temporary venous atrial or ventricular electrical pacing is sometimes indicated to sup-
port the patient during the induction of anesthesia.

Operative Findings

The 152 patients in this series had rheumatic heart disease except one with cystic medial necrosis, aneurysmal dilatation of the sinuses of Valsalva, and aortic regurgitation. Mitral regurgitation in this case was secondary to ruptured chordae tendineae.

The usual aortic valve pathology included commissural fusion, loss of leaflet substance, and thickening of the leaflets at their attached margins. Massive calcification is common with congenital stenosis, but is uncommon in this group. When calcification occurs it may involve the aortic and mitral valves as a single unit, suggesting that the rheumatic process extends into the tissue between the valves. A failure to consider this point during mitral valve resection may cause an obstructing cuff of tissue to be left in situ.

Most of the resected mitral valves had either a combined stenotic and regurgitant lesion or a stenosis with massive calcification. Adequate repair of the mitral valve was possible in only 24 patients with multiple valve disease. They are not included in this series. The decision between repair and resection is determined solely by the operative findings. The mitral valve is not resected for simple dilatation of the annulus as the result of left ventricular failure secondary to aortic valve disease. Many such valves have been encountered in this clinic during isolated aortic valve replacement, but none has required mitral valve replacement. The functional mitral regurgitation and the elevated left atrial pressure usually disappear immediately after the bypass.

Forty-nine patients had sufficiently severe tricuspid valve disease to warrant replacement of the valve. Combined tricuspid stenosis and regurgitation with thickening of the leaflets and the subvalvular mechanism occurred in 25 of the 49 patients. The 22 valves resected for pure regurgitation showed gross evidence of thickening of the leaflets and shortening of the chordae tendineae. Two resected specimens showed pure tricuspid stenosis. None of the 49 specimens had gross calcification.

Four patients had tricuspid replacement after an annuloplasty had failed to correct the regurgitation. An additional 27 patients with thin, delicate tricuspid valve leaflets had significant regurgitation palpated immediately prior to bypass; 20 had decreased their regurgitation following corrective mitral surgery and did not require tricuspid surgery. The remaining seven patients had unchanged persisting regurgitation;
however, a replacement was not performed because of their favorable early clinical course. Three have subsequently required tricuspid replacement to correct persisting right heart failure.

**Operative Technique**

The techniques of isolated mitral and aortic valve surgery and simultaneous multiple valve replacement have been described in previous reports.1–7 Several technical features are important in multiple valve replacement: (1) flexible exposure, (2) prolonged cardiopulmonary bypass, (3) myocardial protection during aortic cross-clamping, and (4) sequence of implantation.

All patients are operated upon through a midline sternotomy incision. Pressures are routinely measured in the right ventricle and both atria. The tricuspid valve is routinely palpated prior to bypass.

The pump prime for prolonged cardiopulmonary bypass consists of citrated blood stored for 1 to 5 days and 20% mannitol solution to a total dose of 2 g/kg of body weight. The osmotic effect of the mannitol shifts excess extracellular fluid into the intravascular space, causing mild hemodilution.8 No other exogenous diluents are used. Initially the patient is heparinized with 3 mg of heparin per kilogram of body weight. An additional 1 mg/kg/hour of bypass is given if the bypass exceeds 2.5 hours. The patient is cooled to 30 C, and the pump flow is reduced. The mean arterial pressure is maintained at approximately 65 mm Hg.

The mitral valve is exposed first. The pericardial reflection between the inferior vena cava and the right inferior pulmonary vein is divided and the posterior interatrial groove is recreated. The ascending aorta is cross-clamped. A small stab incision is made in the exposed anterior wall of the left atrium. The mitral valve is palpated in the partially decompressed, beating heart to differentiate functional insufficiency from organic disease. If the valve requires repair or replacement, the left atrial incision is extended downward between the inferior vena cava and the right inferior pulmonary vein to reach the back of the heart. When exposure is difficult the incision is extended posteriorly toward the left inferior pulmonary vein. Visualization of the mitral valve is facilitated by anoxic relaxation of the myocardium and decompression of the aortic root. Both are achieved by intermittent cross-clamping of the ascending aorta in the absence of significant aortic regurgitation. Air is aspirated from the proximal aortic segment prior to each declamping to prevent coronary air embolus.

Many patients with multiple valve disease have aortic insufficiency and require continuous aortic cross-clamping during aortic and mitral replacement. A transverse aortotomy is made. The coronary arteries are perfused with blood obtained from the oxygenating chamber, cooled to 4 to 6 C by a heat exchanger with circulating ice water, and delivered to the hand-held coronary cannulae at a combined flow of 350 to 400 cc per minute. Three-minute periods of coronary perfusion are repeated every 15 to 20 minutes until the cross clamp is removed. No intrapericardial coolant is employed.

Intermittent cold coronary perfusion allows sufficient myocardial relaxation to expose the mitral valve without injuring the heart by retraction. Sutures are placed in the mitral leaflets and gentle traction brings the valve into view. It is then easy to determine the feasibility of salvaging the valve. If resection is necessary, the septal leaflet is excised as close as possible to the aortic root to prevent a stump of thickened leaflet impinging upon the limited space available for the two prostheses. A definitive-traction suture is placed in the annulus near the posterior commissure. The remainder of the valve is resected, including division of the papillary muscles and chordae tendineae. Double-armed 2-0 Teflon impregnated Dacron sutures are placed in the liberated mitral annulus. Traction upon each succeeding suture is an important key to good exposure.

The selection of a properly sized mitral prosthesis is especially important in patients with combined aortic and mitral disease. The size of the left ventricular cavity is the most important factor in making this selection. The smaller mitral prostheses are more frequently used in these cases than in isolated mitral valve replacement. The mitral prosthesis is held incompetent with a Foley catheter through its orifice until bypass is to be discontinued. When a properly sized mitral prosthesis is in place there should be no impingement upon the aortic outflow tract.

Aortic valve replacement is performed secondly. If the aortic valve is replaced before the mitral, the subsequent exposure of the mitral valve is difficult. The selection of an aortic prosthesis that will pass easily into the aortic root is of prime importance; a too large prosthesis causes difficult placement, malposition, or obstruction around the ball. The prosthesis is anchored in place with 3-0 Teflon impregnated Dacron vertical mattress sutures. The aortotomy is closed, air is evacuated from the proximal aortic root, and the aortic clamp is removed.

In patients with functional tricuspid regurgitation, a decision for replacement is withheld until bypass has been discontinued and the valve is again palpated in the filled beating heart. If
organic tricuspid disease is discovered prior to bypass, defibrillation is delayed until the valve has been explored. With the caval tapes tightened the right atrium is widely opened and the decision is made to resect or repair the valve. Resection is begun by incising the attached margin of the anterior and posterior leaflets and dividing the papillary muscles deep in the right ventricle. A broad, attached margin of the septal leaflets and its chordal supports are left in situ and 3-0 Teflon impregnated Dacron sutures are anchored in this residual tissue to avoid causing heart block. The size of the ventricular cavity is again the most important consideration in selecting the prosthesis of proper size. Care is taken to avoid injury to the right ventricular endocardium by pressing the prosthesis into the decompressed ventricle.

Ventricular pacing wires are routinely implanted before the chest is closed. Atrial pacing wires are implanted in patients who have intact atrioventricular conduction either before operation or after defibrillation. A prophylactic tracheostomy is frequently performed. A high transverse incision helps to avoid communication with the median sternotomy. The bypass time ranged from 2 to 5 hours, with a mean time of 3 hours and 17 minutes. Neither the total bypass time nor the period of aortic cross-clamping with intermittent coronary perfusion appeared to be a significant cause of mortality or morbidity.

Results

Multiple valve replacement has been performed upon 152 patients at this clinic with a 12% operative mortality and a 14% incidence of late death. Table 1 lists the combinations of multiple valve replacement that have been performed, and the early and late incidence of mortality for each combination. These statistics are compared with isolated mitral and aortic replacement. Table 2 compares early and recent results. The 1967 operative mortality of 4% indicates that these patients can be managed with a reasonable operative risk. Figure 1 gives the age distribution of the patients and includes the operative deaths. Thirty-nine patients below 40 years of age have undergone multiple valve replacement without a mortality. These data

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Valve Replacement Mortality September 1960-January 1968</strong></td>
</tr>
<tr>
<td>No. of patients</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Isolated mitral</td>
</tr>
<tr>
<td>Isolated aortic</td>
</tr>
<tr>
<td>Mitral + tricuspid</td>
</tr>
<tr>
<td>Mitral + aortic</td>
</tr>
<tr>
<td>Triple</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

- Table 2

Multiple Valve Replacement June 1962-January 1968

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Operative Deaths</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>1962-66</td>
<td>125</td>
<td>17 (14%)</td>
</tr>
<tr>
<td>1967</td>
<td>27</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Total</td>
<td>152</td>
<td>18 (12%)</td>
</tr>
</tbody>
</table>

- Table 3

Multiple Valve Replacement: Cause of Operative Death, January 1962-January 1968

<table>
<thead>
<tr>
<th>Cause</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low output</td>
<td>8</td>
</tr>
<tr>
<td>Failure to resuscitate</td>
<td>4</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>2</td>
</tr>
<tr>
<td>Thromboemboli</td>
<td>2</td>
</tr>
<tr>
<td>Primary arrhythmia</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal infarction</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
</tr>
</tbody>
</table>

- Table 4

Multiple Valve Replacement: Cause of Late Death Unrelated to Prosthesis, January 1962-January 1968 (134 Operative Survivors)

<table>
<thead>
<tr>
<th>Cause</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial fibrosis</td>
<td>2</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>1</td>
</tr>
<tr>
<td>Electrical pacemaker failure</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
</tr>
</tbody>
</table>

- Table 5

Multiple Valve Replacement: Cause of Late Death Related to Prosthesis, January 1962-January 1968 (134 Operative Survivors)

<table>
<thead>
<tr>
<th>Cause</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary embolus</td>
<td>5</td>
</tr>
<tr>
<td>Cerebral embolus</td>
<td>1</td>
</tr>
<tr>
<td>Thrombotic occlusion</td>
<td>3</td>
</tr>
<tr>
<td>Bacterial endocarditis</td>
<td>1</td>
</tr>
<tr>
<td>Ball variance</td>
<td>3</td>
</tr>
<tr>
<td>Sudden death—no autopsy</td>
<td>2</td>
</tr>
<tr>
<td>Reoperation—cardiac</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
</tr>
</tbody>
</table>
Table 6
Multiple Replacement Late Leak: 12 Cases (16 Leaks) in 112 Survivors

| Successful reoperation | 3 |
| Reoperation—death      | 1 |
| Leak not hemodynamically significant | 8 |
| Total                  | 12 |

are based upon a 100% follow-up of the 152 cases.

Table 3 lists the causes of the operative mortalities. Cardiac pacing, ventilatory assistance, and adequate blood volume have considerably diminished the incidence of low output deaths. Five late deaths were clearly unrelated to the prostheses (table 4). Table 5 lists the late deaths which may have been related to the prostheses. The timing of the late deaths is shown in figure 2.

Complications were common in the early cases surviving multiple valve replacement. The majority were bleeding problems or arrhythmias. Electrical pacing has helped to solve the problem of arrhythmias. The major complications associated with prosthetic valve replacement are sepsis, leak, anemia, thromboembolism, and ball variance. Neither an endocarditis nor a wound infection has occurred in this multiple valve series. Table 6 shows the incidence of late leak and the significance of the leak.

Thromboembolism is the most important late complication of prosthetic valve replacement. The incidence and severity of the thromboembolic complications following...
multiple valve replacement are shown in figure 3. There is no apparent increase in the risk of thromboembolism with multiple replacement as compared to isolated mitral valve replacement. Figure 4 illustrates the timing of the late thromboembolic complications that have been observed. The introduction of the extended cloth prostheses (mitral #6120, and aortic #1200) in 1965 has decreased the incidence of thromboembolic complications from 61% to 7% in isolated mitral replacement, and from 29% to 9% in isolated aortic replacement. It is too early to predict accurately the embolic potential of the completely cloth-covered prostheses model #6300 mitral, and model #2300 aortic), which are now being used clinically. The necessity for long-term anticoagulant therapy is currently being evaluated in a double-blind study with these new prostheses. The majority of the patients who are unable to participate in this study are receiving routine anticoagulant therapy.

The destructive change in the silicone rubber ball, previously reported as ball variance, results from a unique and peculiar infiltration of the silicone rubber with fatty material from the blood. This deforms the ball and may lead to valve failure. Ball variance caused three deaths and five reoperations in multiple valve cases. Two patients had unsuspected mitral ball variance at reoperation 2 years after double valve replacement. After isolated aortic valve replacement the diagnosis of ball variance frequently can be made by auscultation. The opening click of the prosthesis is diminished or absent. Phonocardiography has helped to document this finding. Phonocardiography is crucial in the diagnosis of ball variance after multiple valve replacement because the aortic opening sound may be masked by the closing sound of the mitral prosthesis. A phonocardiogram which demonstrates a marked diminution of the opening sound of the aortic prosthesis in a multiple valve replacement patient is shown in figure 5. Reoperation is necessary if the patient has symptoms suggesting obstruction of the aortic prosthesis or a complete absence of the prosthetic opening sound. The hollow Stellite ball of the current prostheses is designed to avoid this complication.

**Functional Results**

Representative cardiac catheterization findings after multiple valve replacement have been previously reported. Patients with preoperative pulmonary hypertension demonstrate a fall in pulmonary artery pressure. A profound fall is usually observed in the mean left atrial pressure, and despite the frequent use of small size mitral prostheses, the left atrial end-diastolic pressures are usually normal at rest. Left ventricular and systemic arterial pressures generally fail to demonstrate a gradient across the aortic prosthesis. Nine patients studied 6 months after multiple replacement including the tricuspid valve revealed a higher resting cardiac index than their preoperative values and a satisfactory exercise response in all but one patient.

Of the 112 current survivors of multiple valve replacement 100 are living at least 6 months after operation. Sixty-four patients are judged to be class I by the New York Heart Association Classification. They are normally active, free from all cardiac symptoms, and eating a regular diet. Postoperative roentgenograms show a dramatic reduction in cardiac

![Figure 5](http://circ.ahajournals.org/lookup/doi/10.1161/01.CIR.39.4.661)  
*A phonocardiogram of a patient after multiple valve replacement demonstrates “ball variance” of the aortic valve prosthesis. MC, mitral closure; AC, aortic closure; MO, mitral opening; AO, aortic opening. The ratio of amplitude of AO to AC is 0.4; this suggests deterioration of the aortic ball. Successful reoperation verified the diagnosis in this asymptomatic patient.*

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size. Thirty-four patients are judged to be class II. They require exercise restriction but are greatly improved and are managed without severe salt restriction. Postoperative roentgenograms show a reduction in heart size, but mild cardiomegaly usually persist. Two patients remain in class III or IV, and require careful medical management including marked salt restriction and diuretics. Although these patients are improved, they represent unsatisfactory results because of continued cardiomegaly and limited exercise tolerance. Preoperatively they had massive cardiomegaly, severe right ventricular failure, and functional tricuspid regurgitation. This suggests that right ventricular dysfunction is an important factor in the poor results observed in these far-advanced cases. Severe myocardial fibrosis and coronary artery insufficiency are also frequently noted to contribute to a poor result.15

Discussion

The over-all mortality for multiple replacement and for isolated replacement is comparable; however, a slightly greater late mortality is observed following multiple replacement. This result is only possible when all pathologic valves are identified and corrected.

The catheterization pressures may suggest only mild multiple valve disease, but the combined valvular abnormalities may result in marked restriction of performance as determined by cardiac output and arteriovenous oxygen difference with rest and exercise. Supravalvular cineaoortography is of value in uncovering subclinical aortic valve disease. Left ventriculography often demonstrates the anatomy and severity of concomitant mitral valve disease. Coronary angiography in patients over 40 years of age helps identify severe coronary atherosclerosis. A careful preoperative study of hepatic, renal, and pulmonary function is important.

If the patient's condition is precarious, it may be risky to undertake extensive diagnostic studies and the clinical evaluation may be sufficient to define the need for operation. Complete surgical exploration provides the necessary information to determine the nature and the extent of the pathology.

A stenotic aortic valve with an insignificant preoperative pressure gradient may demonstrate marked obstruction and a high gradient after corrective mitral surgery has increased the cardiac output. Direct exploration may reveal a badly damaged valve which belies the mild hemodynamic findings. Uncorrected aortic regurgitation after mitral valve replacement often compromises the late functional result.

Severe aortic valve disease can overshadow coexisting mitral disease, especially in the presence of left ventricular failure with high end-diastolic pressures. In patients with multivalvular disease it may be necessary to expose both the aortic and mitral valves before an accurate diagnosis can be made. The median sternotomy approach offers an excellent exposure for this purpose.

Tricuspid valve replacement was performed in 10% of the mitral replacement group, and in 27% of the mitral and aortic replacement group to make a total of 49 patients. Tricuspid valve disease was not suspected preoperatively in 10 of the 49 patients; six of the 10 had complete right heart catheterization.

Valve replacement is usually necessary for mixed tricuspid disease, although pure or predominate tricuspid stenosis can often be managed by direct-vision commissurotomy. Such a valve must be repalpated to check the regurgitation after terminating the bypass.

Patients with pure tricuspid regurgitation secondary to right ventricular failure and mitral valve disease pose a difficult problem. Massive preoperative tricuspid regurgitation is usually greatly improved after mitral valve replacement. When it persists unchanged, most patients require immediate operative correction if they are to survive and have a satisfactory late result. Annuloplasty is not always effective, and a tricuspid valve replacement is usually necessary. We have not observed significant tricuspid regurgitation present by palpation after bypass which disappeared.
either months or years after corrective mitral surgery. Tricuspid valve replacement is reserved for patients who require a mitral prosthesis for concomitant far-advanced destruction of the mitral valve. If the mitral valve can be repaired satisfactorily, a marginal repair of the tricuspid valve may be acceptable because a later operation is a near certainty. Isolated tricuspid valve replacement for rheumatic valvular heart disease has not been performed in this clinic.

All patients routinely have ventricular pacing wires placed before closure of the chest. Patients with intact atrioventricular conduction either preoperatively or immediately after defibrillation routinely have a transatrial intracavitary pacing lead inserted just above the superior caval-atrial junction and a ground lead in the subcutaneous tissue. Arrhythmias or low cardiac output secondary to bradycardia are managed by atrial pacing at 100-120 per minute with marked improvement. Patients who are unable to follow the atrial pacers usually respond well to ventricular pacing, but the rise in cardiac output is approximately 30% less. Fast arrhythmias have recently been managed by atroventricular or simple ventricular paired pacing, but the experience is too brief to recommend its routine use. This liberal use of electrical pacing has nearly eliminated the use of myocardial depressant drugs in postoperative patients.

References

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