The Course of Patients Following Replacement of the Mitral Valve by a Starr-Edwards Prosthesis

Clinical and Hemodynamic Observations from 18 - 30 Months After Operation

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The surgical treatment of choice at this center for the relief of mitral stenosis with little or no valve calcification is still closed commissurotomy with transventricular dilatation. This approach, however, is not suitable when heavy valvular calcification is present, or when mitral insufficiency is associated with the stenosis, or is present as the sole mitral lesion. In these circumstances, replacement of the valve may be the only method of restoring the deranged hemodynamics towards normal, and thus improving seriously disabled patients. Although prosthetic valves of different designs, a as well as homograft valves b have been used in the mitral area, it is the Starr-Edwards ball valve prosthesis that has been most widely employed.

At this center, 35 patients have had mitral valve replacement by Starr-Edwards prosthesis between June, 1963 and June, 1965. Sixty per cent of these patients, many in the terminal stage of their disease process, had associated tricuspid and/or aortic valve disease. The operations were performed by four cardiac surgeons. The largest number of patients operated on in this period by any one surgeon was 12, with a hospital mortality of 17 per cent.

This report is concerned with the clinical follow-up study and the hemodynamic changes following insertion of a Starr-Edwards ball valve in 13 patients who were operated on early in this series and who have been followed for a period of 18 to 30 months.

Materials and Methods

Thirteen patients in Grade III and IV of the New York Heart Association Classification before operation, were on follow-up for 18 to 30 months following mitral valve replacement. Nine patients had dominant insufficiency and two dominant stenosis, while two patients had equally important insufficiency and stenosis. Eight of the 13 patients had had previous closed mitral commissurotomy and two, a previous mitral annuloplasty (Table 1). Associated tricuspid and/or aortic valve disease was present in six patients.

Homodynamic Assessment

The preoperative hemodynamic assessment was obtained at combined percutaneous retrograde aortic and transeptal left heart catheterization. Insufficiency at mitral, aortic and tricuspid valves was determined by indicator dye dilution technique. Insufficiency at aortic and mitral valves was assessed by cineangiography with injection in the chamber distal to the respective valve. The postoperative assessment was carried out from four to seven months after valve replacement. In addition, all but one of the patients recatheterized were assessed during steady
patients were improved from Grade III or IV before operation to Grade I or II after operation. Three patients had little, or only temporary improvement. These latter three, and two who had been improved, died from five to ten months after operation (see late deaths). Thus, eight of 13 have maintained their clinical improvement over the follow-up period and have returned to normal or near normal activity (Fig. 1).

**Operative Technique**

The valve was excised and replaced under moderate hypothermia using cardiopulmonary bypass. Two patients had a concomitant tricuspid annuloplasty for severe tricuspid insufficiency. Forty-eight to 52 hours after operation, intramuscular heparin was commenced and continued until therapeutic prolongation of the prothrombin time was achieved usingbishydroxycoumarin.

**Results**

**Clinical Status.** The follow-up period extended from 18 to 30 months. Ten of 13

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**Table 1**—Preoperative Assessment in 13 Patients Followed for 18-30 Months After Mitral Valve Replacement

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Grade</th>
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<tr>
<td>Predominant Insufficiency</td>
<td>9</td>
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<td>Mitral Lesion Stenosis</td>
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<td>Predominant Insufficiency + Stenosis</td>
<td>2</td>
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<tr>
<td>Associated Tricuspid and/or Aortic Lesion</td>
<td>6</td>
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<tr>
<td>Associated Tricuspid and/or Aortic Lesion</td>
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<td>Previous Mitral Operations Annuloplasty</td>
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state exercises using a bicycle ergometer at a load of 100 kilogram meters.

**Operative Technique**

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**Results**

**Clinical Status.** The follow-up period extended from 18 to 30 months. Ten of 13

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**Figure 1:** Pre- and postoperative functional status in 13 patients, on follow-up from 18-30 months after mitral valve replacement.

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**Hemodynamics.** Six of the eight surviving patients were restudied from four to seven months after operation. Two were not catheterized (one had sustained chronic brain damage following resuscitation from a cardiac arrest in the postoperative period, and the other had had repeated hospitalization for closure of a mediastinal sinus). One of the six recatheterized had not been studied before operation. This patient had had iatrogenic mitral insufficiency produced when a chordae tendinae was torn during transventricular dilatation for the relief of tight mitral stenosis. Exer-
### Table 2—Pre- and Postoperative Hemodynamic Findings Following Mitral Valve Replacement in Six Patients

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<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Mitral Lesion</th>
<th>Size of Prosthesis</th>
<th>Catheterization</th>
<th>Pressures mm.Hg</th>
<th>Mitral Insufficiency</th>
<th>Cardiac Index L/Min./M²</th>
<th>Comments</th>
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<td>Heart Rate &amp; Rhythm</td>
<td>R. V. Systolic</td>
<td>L. A. Mean</td>
<td>Mean Diastolic Gradient</td>
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<td>A.B.</td>
<td>35</td>
<td>F</td>
<td>M.I.</td>
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<td>J.C.</td>
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<td>J.M.</td>
<td>42</td>
<td>M</td>
<td>M.S.</td>
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1+=Trivial; 2+=mild; 3+=moderate; 4+=severe; M.I.=mitral insufficiency; M.S.=mitral stenosis; AF=atrial fibrillation; SR=sinus rhythm.
Exercise studies were carried out on five of the six patients restudied.

(a) Pressures and Cardiac Output (Table 2). The mean resting left atrial pressure was elevated from 20 - 35 mm.Hg in all patients before operation. It fell to normal or near normal after operation. On exercise there was a rise from 3 - 10 mm.Hg above the resting level (Fig. 2). This was most marked in W. F. in whom a small prosthesis (2M) had been used. In three of five there was a satisfactory rise in cardiac output on exercise. In two, L. B. and D. T., no increase in cardiac output with exercise could be demonstrated. Both patients, however, showed a rise of left ventricular end diastolic pressure (LVEDP). L. B. had a marked myocardial factor which had led to the breakdown of a previous mitral annuloplasty and B. T. was shown to have moderate regurgitation between the mitral annulus and the ring of the prosthetic valve.

The LVEDP, which was elevated in four patients before operation, returned to normal in three.

The mean diastolic gradient between left atrium and ventricle was determined planimetrically. All patients showed a resting gradient ranging from 1.7 to 10.1 mm.Hg after operation. During steady state exercise, this mean gradient rose from 3.1 to 6.9 mm.Hg.

**STARR-EDWARDS MITRAL PROSTHESIS**

**diastolic gradients**

![Graphs showing diastolic gradients before and during exercise for B.T. and J.M.](image)

**Figure 2**: Simultaneous pressure tracings in left atrium and left ventricle in two patients following mitral valve replacement. Patient B. T. (3M prosthesis) had regurgitation through a dehiscence. Note rise in LVEDP on exercise. Patient J. M. (4M prosthesis). Note resting diastolic gradient increase on exercise.
(b) Competence of Prosthesis. In five of the six recatheterized, cineangiocardio-
graphy with injection of dye into the left ventricle demonstrated a minimal jet of
radiopaque dye regurgitating into the left atrium. This jet was limited to early systole
and occurs in the time during which the ball travels from the apex of the cage to
be seated into the prosthetic ring (Fig. 3). This degree of regurgitation cannot be de-
monstrated by indicator dye dilution studies when dye is injected distally, and sampled
proximal to the prosthetic valve. One of the six patients catheterized, however,
showed moderately severe regurgitation be-
tween atrium and ventricle, both on cine-
angiocardiology and by indicator dye
dilution curves. At reoperation, a 1 cm.
long dehiscence was found between the
annulus and the prosthetic ring, and this
was successfully closed. Two other patients
not recatheterized, were shown to have a
similar degree of dehiscence at necropsy.
In one of these no apical pansystolic mur-
mur was present to indicate the presence
of regurgitation.

Late Complications

(a) Systemic Embolization: This oc-
curred in two patients. One took his anti-
coagulant drugs irregularly and sustained
two separate embolic episodes involving the
lower extremities and resulting in intermit-
tent leg claudication. The other had to be
taken off anticoagulant drugs when hemor-
rhage occurred with the onset of serum
hepatitis. One and a half months later,
fatal multiple systolic embolization oc-
curred.

(b) Serum Hepatitis: This occurred in
one patient (also quoted under systemic
embolization). With the onset of hepatic
dysfunction the prothrombin time could
not be controlled and anticoagulants had
to be discontinued.

(c) Ventricular arrhythmia: Two pa-
tients developed repeated bouts of ventric-
ular tachycardia. These attacks were not
associated with low serum potassium levels.
Both died in attacks of ventricular arrhyth-
mania. At necropsy, one of them was found
to have a dehiscence (see competence of
prosthesis). Until the onset of the tachy-
cardia he had been clinically well.
LATE DEATHS

In addition to the two quoted under ventricular arrhythmia and one quoted under systemic embolization, there were two other deaths. These latter two died in congestive failure, one from a marked myocardial factor and the other from regurgitation through a dehiscence (also quoted under competence of prosthesis). These five late deaths occurred from five to ten months after operation. Necropsy studies in four of these patients showed patches of endocardial fibrosis on the left ventricular wall where the cage of the prosthesis impinged during systole.

DISCUSSION

Ten of 13 patients were markedly improved after operation and eight have maintained their improvement during the period of follow-up. Two of the improved and three who were not improved by the operation died.

Those who were recatheterized showed satisfactory hemodynamic correction. Pressures proximal to the valve were reduced to normal or near normal and a normal output was present. Both the mean left atrial pressure and the mean diastolic gradient became elevated in the five patients exercised. In three, exercise was associated with an increased cardiac output suggesting increased flow across the valve, but in two there was no such increase in cardiac output and they showed an elevation of the LVEDP.

Studies by Kedzi et al., estimate the 3M prosthesis to have a ring orifice area of 3.14 sq. cm., but estimate a 10 per cent reduction of this area due to the presence of Teflon cuff, ball and cage. Morrow et al. estimate the hydraulic area of the 3M prosthesis to be 2.54 sq. cm. While these estimated areas suggest some degree of stenosis, when compared to a normal mitral valve area of 5 sq. cm., the clinical results and the hemodynamic findings suggest a very satisfactory correction of the mitral pathology in these severely disabled patients. Moreover, recently reported studies by Braunwald et al. show good results following the use of this prosthesis in a group of patients with pulmonary hypertension and marked elevation of pulmonary vascular resistance. Although this particular group of patients faces a higher operative mortality, they stand to gain marked clinical and hemodynamic improvement.

The incidence of late complications with the use of the ball valve is disturbing. Systemic embolization appears to be the most common complication and has been reported from many centers. Most centers employ longterm and lifetime anticoagulation. The risk of important hemorrhage in patients on longterm anticoagulation, even when the prothrombin time and anticoagulant dosage is controlled in specialized clinics, is real. In the experience of this hospital, the incidence of a major hemorrhage is one per ten patients per patient year of treatment. Moreover, the protection provided by longterm anticoagulation, even with the prothrombin times within the therapeutic range, is by no means complete.

Two patients in the series died from ventricular arrhythmias, namely, tachycardia followed by fibrillation. A case of sudden death, presumably due to an arrhythmia was reported by Ellis, Jr., et al. All in this series who were studied at necropsy showed patches of endocardial fibrosis on the wall of the left ventricle where the cage had traumatized the wall. There may well be an association between the repeated traumatization and the ventricular arrhythmia.

Dehiscence of the prosthetic valve was present in three patients in this series. This was clinically evident in two by the presence of an apical pansystolic murmur. However, in one no such murmur could be heard. All of them had a dehiscence 1 cm. long, demonstrated either at reoperation or at necropsy. Morrow et al. also report the presence of "murmurless regurgitation." While infection may result in dehiscence, this is probably not a com-
mon cause. Thus, it would appear that a patient who fails to improve after operation, or who has an apical pansystolic murmur should have repeat hemodynamic investigation and if a dehiscence is confirmed, should have this closed at reoperation.

Bacterial endocarditis on the prosthetic valves, while not seen in this series, has been reported.1,10,11,12,13

The myocardial factor may be an important and difficult factor to assess, especially in patients with mitral insufficiency. Two such patients in this series had an important myocardial factor present. One, after initial improvement, progressively deteriorated and died in congestive failure five months after operation. The other, a young girl age 21, showed improvement from Grade III or IV to Grade I or II after operation, although the hemodynamic evaluation suggested the presence of an appreciable myocardial factor. The recurrence of low grade rheumatic activity, often suspected clinically, but difficult to prove objectively, may play an important part in determining the clinical picture.

While in a study of this nature, the patients who have not done well tend to attract our detailed attention because the cause for their non-improvement may be remedial, it is important not to overlook the significant number of seriously disabled patients (8 to 13) who have been restored to normal or near normal activity.

SUMMARY

Thirteen patients have been followed from 18 to 30 months after mitral valve replacement by a Starr-Edwards ball valve prosthesis. Ten have been markedly improved and have returned to normal or near normal existence. Two of them, and three who had no improvement died from five to ten months after operation. Late complications include systemic embolization, ventricular arrhythmia and dehiscence of the prosthetic valve permitting regurgitation between left atrium and ventricle.

Failure to improve after operation may be due to regurgitation (sometimes murmurless) or myocardial factor. Despite the late complications seen with this prosthesis, eight of 13 patients have maintained their improvement over the follow-up period.

ACKNOWLEDGMENT: The authors wish to thank Miss J. McKeegan, B.Sc., Mrs. E. Holly and Miss N. Gonzalez for their technical assistance.

REFERENCES

13 GEREEN, A. N., GOURLAY, R. H., KAVANAUGH-GRAY, D.: "Open Heart Surgery for Mitral
PULMONARY REACTIONS DUE TO INHALATION OF ORGANIC ANTIGENS

The author describes two types of allergic reactions due to the inhalation of antigenic organic dusts. The first is an asthma due to an immediate hypersensitivity in the bronchi accompanied by eosinophilia and sometimes by transitory pulmonary infiltrations, and the second, a more slowly developing reaction in the interstitial lung tissue, with the production of epithelioid cell granulomata. In the first type, reaginic antibodies are present and in the cases with pulmonary infiltrations, precipitins as well as reagins are found. Precipitins are present in the second type and may be detected in the patient's serum by immuno-electrophoresis. Discussions of farmer's lung due to Thermopolyspora, fog fever in cows exposed to mouldy hay, diabetics under treatment by inhalation of putrified snuff, pigeon breeders disease, etc., are included.


STUDY OF 194 MALIGNANT BRONCHOGENIC TUMORS IN WOMEN

The authors report a detailed study of 194 malignant tumors of the bronchi in women. All were proved by biopsy. There were 101 secondary, 75 primary and 20 probably primary tumors. Twenty-six per cent of the primary tumors were anaplastic carcinomas as contrasted to 1 per cent of this type found in males. Eighteen of the probably primary tumors were adenocarcinomas and it was found that pleural effusions were encountered more frequently with this type. Of the secondary tumors, 48 were secondary to breast tumors and 29 to tumors of the uterus. Twenty-six per cent of the patients in the primary group were smokers, as compared to 1 per cent in the secondary group. The average age of the patients was 53 years.


INCOMPLETE BLOCK ASSOCIATED WITH SEPTAL INFARCT

The electrical manifestations of incomplete right bundle branch block (IRBBB) with myocardial infarction were studied in ten dogs. The most important changes were recorded in the right unipolar epicardial and precordial leads. The most significant vectorcardiographic changes were observed in the horizontal plane. With IRBBB of advanced degree, the centrifugal branch of the S wave, the loop shifts to the right and behind the 0 point following a right septal infarction. This fact is due to the relative predominance of the postero-septal electrical forces, when the necrosis is localized to the right anterio-septal mass. In second degree right bundle branch block with right septal infarction, the centrifugal branch of the S wave loop can remain in front of the 0 point because of the electrical predominance of the anterolateral regions of the free right ventricular wall. The centrifugal branch of the S wave loop is situated behind and to the right of the 0 point, in first degree right bundle block with right septal infarction. This behavior is due to the relative electrical predominance of the posterobasal regions of the right ventricle.