Left ventricular function after aortic valve replacement¹

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Changes in haemodynamics and in systolic time intervals, early after aortic valve replacement, were studied in a group of 15 patients. Though all the haemodynamic measurements were within normal limits at 44 hours after operation, there was a persistent change in systolic time intervals (shortening of left ventricular ejection time and electromechanical systole, and prolongation of pre-ejection period and increase in the ratio PEP/LVET). The effect of periods of myocardial ischaemia during cardiopulmonary bypass on myocardial function is suggested as the explanation for the changes observed.

Haemodynamic changes in the early postoperative period after open heart surgery have been previously reported (Austen *et al.*, 1966; Carey and Plested, 1972; Fordham and Resnekov, 1967; Kirklin and Theye, 1963; Kloster *et al.*, 1966; Rastelli and Kirklin, 1967). The variable period of reduced cardiac output after cardiopulmonary bypass is influenced by many factors and as a result interpretation of events is difficult. The extent of the effects of bypass and of the ensuing changes in left ventricular performance still remains to be defined. The atraumatic technique of systolic time interval measurement has been used widely in preoperative clinical assessment of left ventricular function, and in some later postoperative studies (Benchimol and Matsuo, 1971; Bonner, Sacks, and Tavel, 1973; Gibson, Broder, and Sowton, 1970; Parisi, Salzman, and Schechter, 1971; Weissler, Lewis, and Leighton, 1972). This report concerns its use in combination with routine haemodynamic measurements in the early period after aortic valve surgery.

Patients and methods

Fifteen patients (14 men, 1 woman) undergoing routine elective aortic valve replacement were studied. The mean age was 48 years with a range from 24 years to 68 years. Clinically, 8 patients had predominant aortic regurgitation and 3 aortic regurgitation alone. The aetiology was rheumatic in 7 patients, congenital in 5, bacterial endocarditis in 2, and syphilis in 1.

Normothermic cardiopulmonary bypass was used

with a Hartmann haemodilution prime and a Temptrol bubble oxygenator (Bentley Laboratories). Bilateral coronary perfusion was used with intermittent ischaemic periods of up to 15 minutes. The mean bypass time was 101 minutes (range from 65 to 176 minutes), and mean ischaemia time was 23 minutes (range from 6 to 45 minutes). In eight patients the aortic valve was replaced by a Starr-Edwards prosthetic valve (model 1260), and in 7 patients by a homograft (antibiotic nutrient preservative as described by Al-Janabi and Ross, 1973).

All patients remained in sinus rhythm throughout the study. No inotropic agents were used in the postoperative period, except for 3 patients who were taking digoxin before operation and afterwards. Serum potassium was monitored and supplements given to maintain serum levels between 4.0 and 5.5 mmol/l. None of the patients required intermittent positive pressure ventilation for more than three hours after operation. There were no hospital deaths and no evidence of myocardial damage was found in the postoperative electrocardiograms.

The preoperative non-invasive study was performed during the afternoon before operation, and the haemodynamic values were measured in the anaesthetic room, before the induction of anaesthesia, after premedication with papaveretum (20 mg) and hyoscine (0.4 mg). All studies were repeated 4, 20, and 44 hours after operation.

The systolic time intervals were determined from the electrocardiogram (lead chosen to show Q wave), the phonocardiogram (usually at the left sternal edge where aortic valve closure (A_2) is most clearly recorded), the external carotid pulse tracing, and respiratory tracing, simultaneously recorded

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on an Elema-Schönander Mingograf 34. The following time intervals were measured: electro-mechanical systole (Q-A₂) and left ventricular ejection time (LVET). The pre-ejection period (PEP) was calculated by subtracting LVET from Q-A₂ and the PEP/LVET ratio was calculated (Weissler *et al.*, 1972); these measurements were corrected for heart rate and sex: Q-A₂ index, LVET index, and PEP index were derived using the regression equation from normals (Weissler, Harris, and Schoenfeld, 1968). As an alternative method of expression, deviation from normal was shown as percentage of predicted value which takes heart rate and sex into account (Weissler and Garrard, 1971).

An arterial cannula was inserted percutaneously into the brachial or radial artery, and a Swan-Ganz catheter into the brachial vein for right heart and pulmonary arterial wedge pressures. After the operation, in addition, a direct left atrial line was left *in situ*, and a venous cannula was placed in the right atrium through the innominate vein. All the pressures were recorded on a Devices M4 Recorder, using Bell and Howell pressure transducers, with the mid-thorax as the reference zero. Cardiac output was measured using the cardiogreen dye-dilution technique, with injection of the dye into the right atrium or pulmonary artery and sampling from the arterial cannula. The reported values are the average of two consecutive determinations. Calculation of forward stroke work index (SWI) was by the following formula:

$$\text{SWI} = \text{PSAP} \times \text{SI} \times 13.6$$

where PSAP is the peak systolic arterial pressure (mmHg), and the SI is forward stroke index (ml/beat per m² BSA). This value underestimates total left ventricular stroke work in the presence of

TABLE 2 *Systolic time intervals before and after aortic valve replacement*

	Before operation	After operation* 4 hours	20 hours	44 hours
PEP index† (ms)	113.5 ± 11.36	168.5 ± 10.76 P<0.0005	163.5 ± 18.79 P<0.0005	157.5 ± 18.09 P<0.0005
LVET index† (ms)	437.1 ± 23.92	360.2 ± 19.83 P<0.0005	348.1 ± 19.42 P<0.0005	350.5 ± 30.34 P<0.0005
Q-A ₂ index† (ms)	550.8 ± 28.35	531.3 ± 18.04 P<0.025	511.5 ± 22.65 P<0.0005	514.8 ± 25.17 P<0.0005
PEP/LVET†	0.271 ± 0.036	0.715 ± 0.150 P<0.0005	0.661 ± 0.123 P<0.005	0.641 ± 0.136 P<0.005

*P values indicate significance of differences between post-operative and preoperative measurements.

†Mean ± SD.

aortic regurgitation because it does not take into account the regurgitant volume, and in the presence of aortic stenosis because it ignores the aortic valve gradient.

Student's *t*-test was used for the analysis of the results.

Results

I: Haemodynamic data (Table 1)

Right atrial and left atrial pressures did not change significantly during the study. Mean arterial pressure was within normal limits and showed no significant change.

Heart rate increased significantly from the pre-operative value throughout the postoperative period, while the cardiac index was reduced post-operatively at 4 hours after operation ($P < 0.001$).

TABLE 1 *Haemodynamic variables before and after aortic valve replacement*

	Before operation	After operation* 4 hours	20 hours	44 hours
Right atrial pressure (mmHg)	6.2 ± 2.3	7.1 ± 3.4	7.1 ± 2.4	7.2 ± 2.5
Left atrial pressure (mmHg)	11.2 ± 8.0	10.4 ± 5.1	11.2 ± 4.4	10.7 ± 5.9
Mean arterial pressure (mmHg)	84.9 ± 15.1	91.7 ± 15.0	84.4 ± 14.7	90.1 ± 11.9
Heart rate (beats/min)	76.8	99.8 P<0.001	88.6 P<0.005	101.4 P<0.001
Cardiac index (l/min per m ² BSA)	3.08 ± 0.77	2.22 ± 0.37 P<0.001	2.62 ± 0.50	2.91 ± 0.65
Stroke index (ml/beat per m ² BSA)	40.9 ± 10.0	23.2 ± 5.7 P<0.001	30.3 ± 5.6 P<0.005	28.6 ± 5.9 P<0.001
Systemic arterial resistance (units)	15.0 ± 4.0	21.4 ± 6.9 P<0.005	16.7 ± 5.1	17.4 ± 3.9
Left ventricular stroke work index (g m/beat per m ² BSA)	81.8 ± 23.7	40.4 ± 11.9 P<0.001	49.2 ± 15.6 P<0.005	48.20 ± 13.0 P<0.005

*P values indicate significance of differences between postoperative and preoperative measurements. Conversion factors from Traditional to SI units: 1 mmHg ≈ 0.133 kPa; 1 unit ≈ 8 Mpa s m⁻³.

FIG. 1 Systolic time intervals as percentages of predicted values (Weissler *et al.*, 1968) before operation, and at 4, 20, and 44 hours after operation. PEP, pre-ejection period; LVET, left ventricular ejection time; Q-A₂, total electromechanical systole; PO, preoperative.

Stroke index was decreased throughout the post-operative period of the study and systemic arterial resistance was increased at 4 hours after operation ($P < 0.005$). Stroke work index was high preoperatively and decreased significantly ($P < 0.005$) to normal values throughout the postoperative period.

Comparing patients who before operation had aortic stenosis with those who had aortic regurgitation, there was no significant difference in these haemodynamic variables and there was no significant difference in postoperative behaviour between patients with Starr-Edwards prosthetic valves and those with aortic homografts (all P values > 0.05).

II: Systolic time intervals

The mean values for the systolic time intervals corrected for heart rate and sex are shown in Table 2. Before operation PEPI is short and LVETI and Q-A₂I are prolonged. The ratio PEP/LVET is also shorter than normal. In the postoperative period PEPI was prolonged and LVETI was shortened; the ratio PEP/LVET was longer than normal and significantly different from the preoperative values. The most abnormal results were seen 4 hours after operation. In Fig. 1, the histograms of the percentages of the predicted values are shown at the four different times of study in all the patients for PEP, LVET, Q-A₂, and PEP/LVET.

Statistical comparison of the group of patients with aortic stenosis before operation with the group with aortic regurgitation, and of the group with Starr-Edwards prostheses with the group with homograft valves, showed no significant differences. The most sensitive variable, PEP/LVET, was correlated with duration of myocardial ischaemia

during cardiopulmonary bypass, and with the total bypass time. In Fig. 2, PEP/LVET at 44 hours is plotted against total bypass time and ischaemic time during operation. Fig. 2b shows that there was no close correlation between total bypass time and PEP/LVET at 44 hours in 15 patients ($r = 0.601$; SEE 16.9). On the other hand, there was a close correlation between ischaemic time and PEP/LVET ($r = 0.923$; SEE 3.71). Further analysis suggested two populations: three patients with ischaemic time less than 10 minutes, and the other 12 patients for whom the correlation between ischaemic time and PEP/LVET was very close ($r = 0.977$; $y = 20.20x + 133.55$) (Fig. 2a).

Discussion

After aortic valve replacement most patients had a normal cardiac index within 24 hours, despite the fact that some were limited functionally by their heart disease before operation; previous reports have shown little difference in the early post-operative haemodynamics between patients with predominant aortic stenosis and those with predominant aortic regurgitation (Austen *et al.*, 1966). Routine haemodynamic monitoring of patients undergoing open heart surgery usually includes measurement of right and left ventricular filling pressures and systemic arterial pressure for 24 to 48 hours after operation in order that complications including heart failure and tamponade can be recognized early and prevented; in addition, cardiac output is often measured. However, these observations do not provide a comprehensive assessment of left ventricular performance. Recently, invasive techniques have been used for the

FIG. 2 (a) Myocardial ischaemic time (min) plotted against pre-ejection period/left ventricular ejection time ratio. Regression equation $y = 20.20x + 133.55$ is calculated omitting 3 patients with ischaemic times of less than 10 minutes. Correlation coefficient $r = 0.977$; SEE 1.31. PEP, pre-ejection period; LEVET, left ventricular ejection time. (b) Total cardiopulmonary bypass time (min) plotted against pre-ejection period/left ventricular ejection time ratio. Correlation coefficient $r = 0.601$; SEE 16.9. PEP, pre-ejection period; LVET, left ventricular ejection time.

assessment of haemodynamic changes during this period, employing catheter tip manometers left in the ventricular cavity (Bolooki, 1973), and electromagnetic flowmeters placed around the aorta (Morrow, Brawley, and Braunwald, 1965; Chamberlain *et al.*, 1974). Systolic time intervals have been shown to correlate well with other measurements of left ventricular performance (Garrard, Weissler, and Dodge, 1970), and are well suited for serial records on individual patients: use of systolic time intervals in the early postoperative period is appropriate provided that they are combined with

routine measurements of left ventricular pump function.

In our group of patients cardiac index and stroke index were low at 4 hours but progressively improved towards 44 hours after operation, changes that have also been shown by others (Austen *et al.*, 1966; Kloster *et al.*, 1966; Rastelli and Kirklin, 1967). Systemic arterial resistance is increased after open heart surgery, and is probably the result of an increase in circulating catecholamines (D. C. Fluck, 1973, personal communication); Rastelli and Kirklin (1967) thought that this was the result of the essentially nonpulsatile flow during cardiopulmonary bypass. We believe that the reduced cardiac index four hours after valve replacement is caused by myocardial depression, as shown by the depression of stroke work index without change in left atrial pressure. As calculated stroke work index is an underestimate in patients with aortic regurgitation, a fall in this index after regurgitation has been abolished by valve replacement is an important observation.

Systolic time intervals are known to be altered in patients with aortic valve disease. When heart failure is absent, there is prolongation of left ventricular ejection time and of electromechanical systole and shortening of the pre-ejection period (Benchimol and Matsuo, 1971; Parisi *et al.*, 1971; Weissler *et al.*, 1972). This was also found in our group of patients before operation; there was no significant difference between patients with aortic stenosis and those with aortic regurgitation. Prolongation of LVET is thought to be caused by increased afterload in aortic stenosis and by increased left ventricular stroke volume in aortic regurgitation (Ahmed *et al.*, 1972; Parisi *et al.*, 1971; Weissler *et al.*, 1972). PEP shortening in aortic valve disease is closely related to the difference between aortic and left ventricular end-diastolic pressures divided by the maximal rate of rise of left ventricular pressure (Parisi *et al.*, 1971). The ratio PEP/LVET is independent of heart rate and sex and has been widely used as a single expression of ventricular performance (Weissler *et al.*, 1968, 1972). After operation there is a complete reversal of the preoperative changes, and this was highly significant ($P < 0.005$). Though the dramatic haemodynamic changes following correction of aortic valve defects would be expected to return the STI to normal, these changes are more profound and are similar to those found in heart failure (Weissler *et al.*, 1968). It is of interest that these changes persist when the cardiac index and stroke work index have returned to normal. Parisi *et al.* (1971) and Benchimol and Matsuo (1971) studied their patients one week to three months after aortic valve

repair or Starr-Edwards valve replacement, and Rothlin and Gattiker (1973) studied a group of patients 24 hours after aortic valve replacement with fascia lata or Björk-Shiley valves. All found prolongation of pre-ejection period and shortening of left ventricular ejection time and electro-mechanical systole; Rothlin and Gattiker also showed that these changes were independent of changes in the cardiac index, which was then low, and that the changes in systolic time intervals correlated well with the duration of the period of ischaemic hypothermic cardiac arrest. Our data confirms their results (Fig. 2).

However, other factors must be considered in the appreciation of these changes in the systolic time intervals after operation. Dependence of systolic time intervals on preload and afterload is well known (Ahmed *et al.*, 1972; Weissler *et al.*, 1972). In our group of patients, preload assessed by left atrial pressure did not change. Afterload was relatively constant after operation but clearly the changes from the preoperative values were different in aortic stenosis and aortic regurgitation. Left ventricular pump performance, as judged by cardiac index and stroke work index, was within normal limits at 44 hours after operation in this study, but systolic time intervals remained abnormal suggesting that there was persisting depression of left ventricular function.

The effects of anaesthesia are unlikely to explain these changes in systolic time intervals. Anaesthetic agents are known to depress left ventricular performance, and to decrease LVET and $Q-A_2$ and prolong PEP during induction of anaesthesia (Blackburn *et al.*, 1973), but no prolonged effect has been shown. Catecholamine release is also known to alter the systolic time intervals in a similar manner to that shown here (Harris, Schoenfeld, and Weissler, 1967), but is accompanied by haemodynamic changes which have not been shown in our patients beyond 4 hours after operation. Lastly, the effect of cardiopulmonary bypass on myocardial function remains a possible explanation. It has been shown both experimentally and in man that there are deleterious effects of cardiopulmonary bypass on myocardial metabolism and structure that could account for the persistence of abnormalities in some of the variables commonly measured to assess ventricular function (Benzing *et al.*, 1970; Braimbridge *et al.*, 1973; Darracott *et al.*, 1973; Isom *et al.*, 1973; Jenkins, Branthwaite, and Bradley, 1973; Stemmer *et al.*, 1973). Thus using systolic time intervals, we have shown an impairment of left ventricular performance up to 44 hours after aortic valve replacement, whereas this is not apparent beyond 4 hours after operation with

routine methods of assessment of left ventricular pump function. Furthermore, the effects upon the myocardium of the periods of ischaemia used during cardiopulmonary bypass could explain this observation; this is supported by the close correlation between the ischaemic period during bypass and PEP/LVET 44 hours after operation (Fig. 2a). Cardiopulmonary bypass alone, without ischaemia, is shown in Fig. 2b to be unlikely to be a significant factor. Though the abnormality of PEP/LVET suggests myocardial depression, correlation of this finding with conventional invasive measures of left ventricular function is at present lacking.

Further studies on this subject will be necessary to clarify the influence of cardiopulmonary bypass and intermittent myocardial ischaemia on myocardial metabolism and function, and the relation between the altered systolic time intervals and more sophisticated measurements of left ventricular function.

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References

- Ahmed, S. S., Levinson, G. E., Schwartz, C. J., and Ettinger, P. O. (1972). Systolic time intervals as measures of the contractile state of the left ventricular myocardium in man. *Circulation*, **46**, 559.
- Al-Janabi, N., and Ross, D. N. (1973). Enhanced viability of fresh aortic homografts stored in nutrient medium. *Cardiovascular Research*, **7**, 817.
- Austen, W. G., Corning, H. B., Moran, J. M., Sanders, C. A., and Scannell, J. G. (1966). Cardiac hemodynamics immediately following aortic valve surgery. *Journal of Thoracic and Cardiovascular Surgery*, **51**, 461.
- Benchimol, A., and Matsuo, S. (1971). Ejection time before and after aortic valve replacement. *American Journal of Cardiology*, **27**, 244.
- Benzing, G., Helmsworth, J., Stockert, J., and Kaplan, S. (1970). Human myocardial performance during surgical treatment of cardiac defects. *Journal of Thoracic and Cardiovascular Surgery*, **59**, 800.
- Blackburn, J. P., Conway, C. M., Davies, R. M., Enderby, G. E. H., Edridge, A. W., Leigh, J. M., Lindop, M. J., Phillips, G. D., and Strickland, D. A. P. (1973). Valsalva responses and systolic time intervals during anaesthesia and induced hypotension. *British Journal of Anaesthesia*, **45**, 704.
- Bolooki, H. (1973). Prolonged left ventricular pressure monitoring by a catheter transducer. *Surgery*, **73**, 97.
- Bonner, A. J., Jr., Sacks, H. N., and Tavel, M. E. (1973). Assessing the severity of aortic stenosis by phonocardiography and external carotid pulse recordings. *Circulation*, **48**, 247.
- Braimbridge, M. V., Darracott, S., Clement, A. J., Bitensky, L., and Chayen, J. (1973). Myocardial deterioration during aortic valve replacement assessed by cellular biological tests. *Journal of Thoracic and Cardiovascular Surgery*, **66**, 241.

- Carey, J. S., and Pleded, W. G. (1972). Immediate hemodynamic response to correction of cardiac valvular lesions. *Annals of Thoracic Surgery*, **13**, 311.
- Chamberlain, J. H., Williams, B. T., Rickards, A. F., and Yate, A. K. (1974). The use of the extractable electromagnetic flowprobe in cardiac surgical patients postoperatively. In *First World Congress on Intensive Care, June 1974, London—Scientific Abstracts*. p. 33. Ed. by I. M. Ledingham. Intensive Care Society, Glasgow.
- Darracott, S., Braimbridge, M. V., Bitensky, L., and Chayen, J. (1973). Myocardial deterioration during perfusion of isolated dog heart assessed by cellular biological tests. *Journal of Thoracic and Cardiovascular Surgery*, **66**, 247.
- Fordham, R. M. M., and Resnekov, L. (1967). Circulatory changes resulting from increasing the venous filling pressure by transfusion following aortic valve homograft replacement. *Cardiovascular Research*, **1**, 159.
- Garrard, C. L., Jr., Weissler, A. M., and Dodge, H. T. (1970). The relationship of alterations in systolic time intervals to ejection fraction in patients with cardiac disease. *Circulation*, **41**, 455.
- Gibson, D. G., Broder, G., and Sowton, E. (1970). Phonocardiographic method of assessing changes in left ventricular function after Starr-Edwards replacement of aortic valve. *British Heart Journal*, **32**, 142.
- Harris, W. S., Schoenfeld, C. D., and Weissler, A. M. (1967). Effects of adrenergic receptor activation and blockade on the systolic preejection period, heart rate, and arterial pressure in man. *Journal of Clinical Investigation*, **46**, 1704.
- Isom, O. W., Kutin, N. D., Falk, E. A., and Spencer, F. C. (1973). Patterns of myocardial metabolism during cardiopulmonary bypass and coronary perfusion. *Journal of Thoracic and Cardiovascular Surgery*, **66**, 705.
- Jenkins, B. S., Branthwaite, M. A., and Bradley, R. D. (1973). Cardiac function after open heart surgery: relationship between the performance of the two sides of the heart. *Cardiovascular Research*, **7**, 297.
- Kirklin, J. W., and Theye, R. A. (1963). Cardiac performance after open intracardiac surgery. *Circulation*, **28**, 1061.
- Kloster, F. E., Bristow, J. D., Starr, A., McCord, C. W., and Griswold, H. E. (1966). Serial cardiac output and blood volume studies following cardiac valve replacement. *Circulation*, **33**, 528.
- Morrow, A. G., Brawley, R. K., and Braunwald, E. (1965). Effects of aortic regurgitation on left ventricular performance. Direct determinations of aortic blood flow before and after valve replacement. *Circulation*, **31**, Suppl. I, 80.
- Parisi, A. F., Salzman, S. H., and Schechter, E. (1971). Systolic time intervals in severe aortic valve disease: changes with surgery and hemodynamic correlations. *Circulation*, **44**, 539.
- Rastelli, G. C., and Kirklin, J. W. (1967). Hemodynamic state early after replacement of aortic valve with ball-valve prosthesis. *Surgery*, **61**, 873.
- Rothlin, M., and Gattiker, K. (1973). Evaluation de la fonction myocardique. *Archives des Maladies du Cœur et des Vaisseaux*, **66**, 749.
- Stemmer, E. A., McCart, P., Stanton, W. W., Thibault, W., Dearden, L. S., and Connolly, J. E. (1973). Functional and structural alterations in the myocardium during aortic cross-clamping. *Journal of Thoracic and Cardiovascular Surgery*, **66**, 754.
- Weissler, A. M., and Garrard, C. L. (1971). Systolic time intervals in cardiac disease (I). *Modern Concepts of Cardiovascular Disease*, **40**, 1.
- Weissler, A. M., Harris, W. S., and Schoenfeld, C. D. (1968). Systolic time intervals in heart failure in man. *Circulation*, **37**, 149.
- Weissler, A. M., Lewis, R. P., and Leighton, R. F. (1972). The systolic time intervals as a measure of left ventricular performance in man. In *Progress in Cardiology*, Vol. 1, p. 155. Ed by P. N. Yu and J. F. Goodwin. Lea and Febiger, Philadelphia.

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