REVIEW ARTICLE

Assessment of chronic aortic valve disease in adults

A. D. HARRIES
M.A., M.R.C.P.

B. E. GRIFFITHS
M.B., B.Ch., M.R.C.P.

University Hospital of Wales, Heath Park, Cardiff

Summary

Chronic aortic valve disease is often tolerated for a long period of time with little in the way of symptoms, but once symptoms develop, the downhill course is often rapid. Medical therapy may alleviate symptoms of congestive heart failure and angina, but does not alter the natural history of the disease. The recent advances of cardiac surgery have, however, considerably improved the prognosis of most patients. Some patients with aortic regurgitation, though, will develop progressive congestive heart failure despite aortic valve replacement. Others with severe aortic stenosis will die suddenly while awaiting surgery as will a small number who previously had been asymptomatic. The information that comes from cardiac catheterization as well as the non-invasive investigation of cardiological disease, greatly enhanced by the introduction of the echocardiogram, has provided the physician with a better understanding of the particular problems in question and, therefore, the potential to solve them. This article aims to review the means by which high-risk groups can be identified, in order that their outlook may be improved especially with respect to the timing of surgical intervention.

Aortic regurgitation

Introduction

Chronic aortic regurgitation is an important form of valvular heart disease which may result from a number of pathological mechanisms which include those due to rheumatic involvement, connective tissue disorders, Marfan's syndrome and syphilitic aortitis. Patients with aortic regurgitation often remain asymptomatic until the fourth or fifth decade (Goldschlager *et al.*, 1973) and, often, 7-10 years can elapse between making the diagnosis and the onset of symptoms (Segal, Harvey and Hufnagel, 1956). When symptoms develop, they are those of left ventricular disease, with breathlessness being the most prominent, although chest pain and syncope may also commonly occur. The physical signs are characteristic—the main features being the

'collapsing pulse' and the early diastolic murmur heard maximally down the left sternal edge.

Clinical features and prognosis

In addition to identifying the presence of aortic regurgitation, there has to be some estimate of its severity. Moderate to severe regurgitation is usually associated with a wide pulse pressure, cardiomegaly and peripheral arterial signs of which Duroziez's sign is particularly useful. With no surgical treatment, mild regurgitation is well tolerated with a 10-year survival rate of 85-95% (Hegglin, Scheu and Rothlin, 1968) whereas the more severe lesion throws a greater burden on the heart with a 10-year survival rate of approximately 50% (Rapaport, 1975). Younger patients, however, who are diagnosed with severe regurgitation in their early twenties seem to fare better with a 10-year survival rate of approximately 60% and a 20-year survival rate of 45% (Bland and Wheeler, 1957).

Particular symptoms appear to relate to prognosis. Fifty per cent. of patients who do not have surgery will succumb 5 years after the onset of angina and 2 years after the onset of left ventricular failure (Dexter, 1969). Congestive heart failure especially has a bad prognosis, 50% of patients being dead 6 months after the onset (Dexter, 1969) and 90% within 2 years of diagnosis (Massell, Amezcua and Czoniczer, 1966). On physical examination, a pulse pressure of 100 mmHg or more and a diastolic pressure of <40 mmHg are also adverse prognostic indicators (Massell *et al.*, 1966; Spagnuolo *et al.*, 1971).

The chest X-ray and the electrocardiogram (ECG) can likewise be useful in assessing prognosis. Significant aortic regurgitation is usually accompanied by cardiac enlargement on the chest X-ray. A cardiothoracic ratio >0.6 helps to identify those in an asymptomatic group who are more likely to develop symptoms and to have an overall increased mortality rate (Massell *et al.*, 1966; Spagnuolo *et al.*, 1971; Smith *et al.*, 1976). The presence on the ECG

of left ventricular hypertrophy and the presence of arrhythmias such as a long PR interval, atrial fibrillation and ventricular premature beats are unfavourable findings, and are also associated with an overall increased mortality rate (Spagnuolo *et al.*, 1971; Smith *et al.*, 1976). Furthermore, a pre-operative ECG score of 6 or more, based on the points system devised by Romhilt and Estes (1968) for the diagnosis of left ventricular hypertrophy is associated with an increased postoperative mortality (Hirshfeld *et al.*, 1974).

Exercise testing until exhaustion or the development of symptoms is often used as an index of cardiac function in the management of patients with a variety of cardiac disorders, and its use in patients with aortic regurgitation is no exception. In symptomatic patients with severe aortic regurgitation, Bonow *et al.* (1980) showed that all the patients completing stage I of their protocol survived aortic valve replacement and were alive 3 years later compared with a 68% survival rate in those failing to complete stage I.

Echocardiography, which employs pulses of high frequency sound waves (ultrasound), has provided physicians with a safe, non-invasive means of studying cardiac structures and their motions. M-mode echocardiography has recently also been found useful in assessing the prognosis of patients with aortic regurgitation. With the ultrasound beam passing through the left ventricle just caudal to the tips of the mitral valve leaflets, it is possible to measure left ventricular cavity size and, in particular, the left ventricular end-systolic dimension (LVESD) and the left ventricular end-diastolic dimension (LVEDD) (Fig. 1). In patients with severe aortic regurgitation who were asymptomatic at the time of presentation, it was found that 80% whose LVESD was >55 mm developed symptoms within a 3-year period severe enough to warrant surgery compared with 20% whose LVESD was <55 mm (Henry *et al.*, 1980c). In symptomatic subjects before surgery, a LVESD greater than 55 mm along with a fractional shortening (FS) less than 25% (Fig. 1) was associated with a high risk of sustaining

Fig. 1. Endocardiogram of the left ventricle.

Left ventricular end-diastolic dimension (LVEDD) = distance between the left side of the interventricular septum (IVS) and the posterior left ventricular endocardium (LVPW) in end diastole. This corresponds to the onset of the Q wave of the ECG (normal 35–56 mm).

Left ventricular end-systolic dimension (LVESD) = distance between the left side of the IVS and posterior left ventricular endocardium taken at the onset of the first high frequency vibration of the second heart sound (S2) on a simultaneously recorded phonocardiogram (Phono) (normal 25–41 mm).

Fractional shortening (FS) of the left ventricle—an index of left ventricular function is calculated from the following equation:

$$\frac{\text{LVEDD} - \text{LVESD}}{\text{LVEDD}} \times 100.$$

CW = chest wall; RV = right ventricular cavity; IVS = interventricular septum; LV = left ventricular cavity.

congestive heart failure postoperatively and of subsequently dying (Henry *et al.*, 1980b).

At cardiac catheterization, aortography allows the diagnosis of aortic regurgitation to be confirmed, and associated mitral valve disease can be excluded by appropriate measurements. Left ventricular pressures are usually normal until late in the disease, and it is therefore not surprising that a raised left ventricular end-diastolic pressure or a raised pulmonary artery wedge pressure is associated with an increased postoperative mortality rate—a consequence of advanced disease (Hirshfeld *et al.*, 1974; Henry *et al.*, 1980b).

Indications for operation

The development of symptoms in patients with moderate to severe aortic regurgitation should be an indication for aortic valve replacement. Most patients do well postoperatively, although some do succumb at operation and some succumb later from congestive heart failure. Echocardiographic and angiographic data support the concept that this latter group of patients develop irreversible myocardial changes, either before or concomitant with the onset of symptoms that lead to operation (Cohn *et al.*, 1974; Henry *et al.*, 1980b; Bonow *et al.*, 1980). Patients with ventricular dysfunction (LVESD >55 mm and FS <25%) who do badly postoperatively often show no reduction in LVESD postoperatively and often have a LVESD >70 mm at the 6-month postoperative assessment (Bonow *et al.*, 1980; Henry *et al.*, 1980b). This is in contrast to those patients who, although they show pre-operative echocardiographic evidence of left ventricular dysfunction, do well postoperatively, for they tend to show a significant reduction in LVESD in the postoperative period, implying that their myocardial damage is reversible. These patients can sometimes be identified pre-operatively because they tend to have a good exercise tolerance (Bonow *et al.*, 1980).

These facts underline the problem that faces the physician when confronted by a patient with severe aortic regurgitation who is nevertheless asymptomatic. If surgery is delayed until the onset of significant symptoms then, for some patients, the operation will fail as a result of irreversible myocardial changes. On the other hand, valve replacement in all asymptomatic patients would result in operative death or prosthetic valve complications in many patients who would otherwise have been asymptomatic for many years. The dilemma has been solved at one centre (Henry *et al.*, 1980c) by using the echocardiogram to determine the optimal time of aortic valve replacement. Asymptomatic patients with a LVESD >55 mm are referred for aortic valve replacement before the onset of symptoms.

The rationale for this is that these patients have developed ventricular systolic dysfunction but that it is not yet irreversible, and indeed this group have a mortality rate far less than that of patients with similar echocardiographic dimensions in whom operation has been delayed until the onset of symptoms. It must be emphasized, however, that this is not a proved criterion by which to make decisions on surgical treatment, and further research would need to be carried out before general acceptance of such a quantitative formula (O'Rourke and Crawford, 1980).

The asymptomatic patient with severe aortic regurgitation needs careful follow-up. A widening of the pulse pressure and a reduction in exercise tolerance, which is best measured by an objective method, would cause concern. If these findings were supported by an increase in size of the heart on chest X-ray, especially a CT ratio >0.6, electrocardiographic evidence of left ventricular hypertrophy and/or arrhythmias and unfavourable echocardiographic parameters, especially LVESD >55 mm and FS <25%, then the need for specialist advice and possible surgery is indicated.

Aortic stenosis

Introduction

Valvar aortic stenosis in adults is usually due to calcification of a bicuspid valve, rheumatic involvement or degenerative disease. The disease may present at any time in life, although it is commonest in elderly males with symptoms not usually becoming manifest until the 6th decade (Takeda, Warren and Holzman, 1963; Ross and Braunwald, 1968). The classical symptoms are those of breathlessness, chest pain and syncope, and the characteristic physical signs are a slow rising carotid pulse associated with an ejection systolic murmur. Patients with aortic stenosis have a tendency to sudden death. The incidence in symptomatic patients has been variably reported at 14% (Campbell, 1968) to 70% (Mitchell *et al.*, 1954). Asymptomatic patients are also not immune (Frank, Johnson and Ross, 1973), and one retrospective study found that 5% of all patients dying suddenly with aortic stenosis had been asymptomatic (Ross and Braunwald, 1968). Among the various mechanisms postulated, cardiac arrhythmias are probably the most important.

Clinical features and prognosis

Moderate to severe aortic stenosis in adults has a poor prognosis in the absence of surgical treatment, with a 5-year mortality rate of approximately 50% and a 10-year mortality rate of 90% (Frank *et al.*, 1973). Once symptoms develop 50% of the patients are dead within 2 years (Bergeron *et al.*, 1954), and 80% within 4 years (Ross and Braunwald, 1968).

Symptoms of angina, syncope, exertional dyspnoea and heart failure are associated in that order with a progressively worse prognosis (Takeda *et al.*, 1963).

Unlike the case with aortic regurgitation, non-invasive investigations which include the chest X-ray, ECG and echocardiogram are on the whole not helpful in identifying which patients have a high mortality rate and which patients might be expected to do badly postoperatively, except in so far as to help the physician decide on the severity of the valvar obstruction (Hirshfeld *et al.*, 1974; Henry *et al.*, 1980a). Systolic gradients measured across the aortic valve at cardiac catheterization also do not correlate well with mortality rate (Frank *et al.*, 1973), but perhaps this is not surprising because as the heart begins to fail, so the cardiac output diminishes, and the gradient can therefore fall to levels not regarded as indicating severe stenosis.

The incidence of sudden death in symptomatic patients appears to relate to the severity of the valvar obstruction (Johnson, 1971). In Johnson's study, 21% of those with severe outflow tract obstruction died suddenly compared with no sudden deaths in patients whose lesions were considered to be mild or moderate. Cardiac catheterization in patients considered for surgery may be useful in this respect in identifying who is at risk of sudden death pre-operatively and therefore in urgent need of valve replacement. A raised pulmonary artery wedge pressure, and severe pulmonary hypertension associated with angiographic evidence of left ventricular failure are markers for sudden pre-operative death (Matthews *et al.*, 1974; McHenry *et al.*, 1979). Although severe pulmonary hypertension is uncommon, a recent study showed that 11% of patients with lone aortic valve disease, who had been considered for surgery, had pulmonary artery systolic pressures of 60 mmHg or more (Basu *et al.*, 1978).

Indications for surgery

For the middle-aged symptomatic patient with severe aortic stenosis there is no doubt that aortic valve replacement prolongs life (Selzer, 1976). In mild cases, surgical treatment is not indicated and medical treatment is usually unnecessary. As with aortic regurgitation the complete diagnosis of aortic stenosis depends not only on recognizing the condition but also on estimating its severity. In the presence of a normal cardiac output a systolic gradient from left ventricle to aorta of 50 mmHg or more signifies that the obstruction is severe, and this is often associated with clinical manifestations that include a small anacrotic pulse, a single or paradoxically split, second heart sound in the absence of left bundle branch block, and ECG evidence of left

ventricular hypertrophy (Wood, 1958). These signs are not always reliable, however, especially when left ventricular dysfunction occurs (Hancock and Abelman, 1957; Wagner *et al.*, 1977). As the cardiac output falls, the characteristic murmur becomes softer or disappears, the slow rising pulse is more difficult to appreciate, and the clinical picture becomes that of a low cardiac output with heart failure. In this situation it is easy to misdiagnose cardiomyopathy or mitral regurgitation. In this sort of case it is important to identify a surgically remediable condition, and the correct diagnosis can be made in most cases if the physician remembers to look for aortic valve calcium on the lateral chest X-ray, to screen the aortic valve for calcium radiologically and to look for abnormal aortic valve echoes on the echocardiogram where the latter investigation is available (Morgan and Hall, 1979). Again, although severe aortic stenosis is often associated with ECG evidence of left ventricular hypertrophy, this is not always so, and sometimes the ECG can be completely normal (Sanders and Friedlich, 1964).

Accepting these limitations, a critical analysis of useful clinical signs has shown that a slow upstroke carotid pulse, a thrusting left ventricular impulse, radiological calcium in the aortic valve, and Q wave inversion in the ECG correlate well with the presence of severe aortic stenosis (Eddleman *et al.*, 1973). In the presence of normal ventricular function, a formula has also been worked out to calculate left ventricular systolic pressure by echocardiography and hence provide a non-invasive means of investigating the severity of outflow tract obstruction (Bennett, Evans and Raj, 1975; Schwartz *et al.*, 1978).

All patients with moderate to severe aortic stenosis who are symptomatic should be considered for specialist advice and surgery. These patients, moreover, are at risk of sudden death, and the pressure measurements obtained from cardiac catheterization should indicate which individuals need urgent valve replacement. Most patients showing evidence of poor left ventricular function pre-operatively would be expected to improve with surgery (Thompson *et al.*, 1979). Where there is failure of improvement of myocardial function, then there is frequently to be found associated coronary artery disease (Linhart *et al.*, 1968; Thompson *et al.*, 1979).

Patients who are asymptomatic with severe aortic stenosis show an increased incidence of sudden death (Ross and Braunwald, 1968; Frank *et al.*, 1973) and, if they are followed-up, almost invariably develop symptoms within one or 2 years (Gibson, 1978). It would seem logical to advise surgery for these patients at centres where the mortality rate for aortic valve replacement is < 5%

Acknowledgment

The authors thank Dr D. Sheridan for his help in preparing the manuscript.

References

- BASU, B., CHERIAN, G., KRISHNASWAMI, S., SUKUMAR, I. & STANLEY, J. (1978) Severe pulmonary hypertension in advanced aortic valve disease. *British Heart Journal*, **40**, 1310.
- BENNETT, D.H., EVANS, D.W. & RAJ, M.V.J. (1975) Echocardiographic left ventricular dimensions in pressure and volume overload. Their use in assessing aortic stenosis. *British Heart Journal*, **37**, 971.
- BERGERON, J., ABELMANN, W.H., VASQUEZ-MILAN, H. & ELLIS, L.B. (1954) Aortic stenosis—clinical manifestations and course of the disease. Review of 100 proved cases. *Archives of Internal Medicine*, **94**, 911.
- BLAND, E.F. & WHEELER, E.O. (1957) Severe aortic regurgitation in young people. *New England Journal of Medicine*, **256**, 667.
- BONOW, R.O., BORER, J.S., ROSING, D.R., HENRY, W.L., PEARLMAN, A.S., MCINTOSH, C.L., MORROW, A.G. & EPSTEIN, S.E. (1980) Pre-operative exercise capacity in symptomatic patients with aortic regurgitation as a predictor of postoperative left ventricular function and long term prognosis. *Circulation*, **62**, 1280.
- CAMPBELL, M. (1968) Calcific aortic stenosis and congenital bicuspid aortic valves. *British Heart Journal*, **30**, 606.
- COHN, P.F., GORLIN, R., COHN, L.H. & COLLINS JR, J.J. (1974) Left ventricular ejection fraction as a prognostic guide in surgical treatment of coronary and valvular heart disease. *American Journal of Cardiology*, **34**, 136.
- DEXTER, L. (1969) Evaluation of the results of cardiac surgery. In: *Modern Trends in Cardiology* 2nd series, p. 311. Butterworth & Company, London.
- EDDLEMAN JR, E.E., FROMMEYER, W.B., LYLE, D.P., BANCROFT, W.H. & TURNER, M.E. (1973) Critical analysis of clinical factors in estimating severity of aortic valve disease. *American Journal of Cardiology*, **31**, 687.
- FRANK, S., JOHNSON, A. & ROSS JR, J. (1973) Natural history of valvular aortic stenosis. *British Heart Journal*, **35**, 41.
- GIBSON, D.G. (1978) Valvar disease. In: *Price's Textbook of the Practice of Medicine*, 12th edn, p. 748. Oxford Medical Publications, Great Britain.
- GOLDSCHLAGER, N., PFEIFER, J., COHN, K., PORRER, R. & SELZER, A. (1973) The natural history of aortic regurgitation: a clinical and hemodynamic study. *American Journal of Medicine*, **54**, 577.
- HANCOCK, E.W. & ABELMANN, W.H. (1957) A clinical study of brachial artery pulse form with special reference to the diagnosis of aortic valvular disease. *Circulation*, **16**, 572.
- HEGGLIN, R., SCHEU, H. & ROTHLIN, M. (1968) Aortic insufficiency. *Circulation*, **38** (Suppl.), V-77.
- HENRY, W.L., BONOW, R.O., BORER, J.S., KENT, K.M., WARE, J.H., REDWOOD, D.R., ITZCOITZ, S.B., MCINTOSH, C.L., MORROW, A.G. & EPSTEIN, S.E. (1980a) Evaluation of aortic valve replacement in patients with valvular aortic stenosis. *Circulation*, **61**, 814.
- HENRY, W.L., BONOW, R.O., BORER, J.S., WARE, J.H., KENT, K.M., REDWOOD, D.R., MCINTOSH, C.L., MORROW, A.G. & EPSTEIN, S.E. (1980b) Observations on the optimum time for operative intervention for aortic regurgitation. I. Evaluation of the result of aortic valve replacement in symptomatic patients. *Circulation*, **61**, 471.
- HENRY, W.L., BONOW, R.O., ROSING, D.R. & EPSTEIN, S.E. (1980c) Observations on the optimum time for operative intervention for aortic regurgitation. II. Serial echocardiographic evaluation of asymptomatic patients. *Circulation*, **61**, 484.
- HIRSHFELD, J.W., EPSTEIN, S.E., ROBERTS, A.J., GLANCY, D.L. & MORROW, A.G. (1974) Indices predicting long-term survival after valve replacement in patients with aortic regurgitation and patients with aortic stenosis. *Circulation*, **50**, 1190.
- JOHNSON, A.M. (1971) Aortic stenosis, sudden death and the left ventricular baro receptors. *British Heart Journal*, **33**, 1.
- LINHART, J.W., DE LA TORRE, A., RAMSEY, H.W. & WHEAT JR, M.W. (1968) The significance of coronary artery disease in aortic valve replacement. *Journal of Thoracic and Cardiothoracic Surgery*, **55**, 811.
- MASSELL, B.F., AMEZCUA, F.J. & CZONICZER, G. (1966) Prognosis of patients with pure or predominant aortic regurgitation in the absence of surgery. *Circulation*, **34** (Suppl.), III-164.
- MATTHEWS, A.W., BARRITT, D.W., KEEN, G.E. & BELSEY, R.H. (1974) Pre-operative mortality in aortic stenosis. *British Heart Journal*, **36**, 101.
- MC HENRY, M.M., RICE, J., MATLOF, H.J. & FLAMM, M.D. (1979) Pulmonary hypertension and sudden death in aortic stenosis. *British Heart Journal*, **41**, 463.
- MITCHELL, A.M., SACKETT, C.H., HUNZICKER, W.J. & LEVINE, S.A. (1954) The clinical features of aortic stenosis. *American Heart Journal*, **48**, 684.
- MORGAN, D.J. & HALL, R.J. (1979) Occult aortic stenosis as cause of intractable heart failure. *British Medical Journal*, **1**, 784.
- O'ROURKE, R.A. & CRAWFORD, M.H. (1980) Editorial: Timing of valve replacement in patients with chronic aortic regurgitation. *Circulation*, **61**, 493.
- RAPAPORT, E. (1975) Natural history of aortic and mitral valve disease. *American Journal of Cardiology*, **35**, 221.
- ROMHILT, D.W. & ESTES JR, E.H. (1968) A point score system for the ECG diagnosis of left ventricular hypertrophy. *American Heart Journal*, **75**, 752.
- ROSS JR, J. & BRAUNWALD, E. (1968) Aortic stenosis. *Circulation*, **37-38** (Suppl.), V-61.
- SANDERS, C.A. & FRIEDLICH, A.L. (1964) Misleading electrocardiographic findings in severe aortic stenosis. *Medicine*, **43**, 393.
- SCHWARTZ, A., VIGNOLA, P.A., WALKER, H.J., KING, M.E. & GOLDBLATT, A. (1978) Echocardiographic estimation of aortic valve gradient in aortic stenosis. *Annals of Internal Medicine*, **89**, 329.
- SEGAL, J., HARVEY, W.P. & HUFNAGEL, C. (1956) A clinical study of one hundred cases of severe aortic insufficiency. *American Journal of Medicine*, **21**, 200.
- SELZER, A. (1976) Cardiac valve replacement: an unanswered question. *American Journal of Cardiology*, **37**, 322.
- SMITH, H.J., NEUTZE, J.M., ROCHE, A.H.G., AGNEW, T.M. & BARRATT-BOYES, B.G. (1976) The natural history of rheumatic aortic regurgitation and the indications for surgery. *British Heart Journal*, **38**, 147.
- SPAGNUOLO, M., KLOTH, H., TARANTA, A., DOYLE, E. & PASTERNAK, B. (1971) Natural history of rheumatic aortic regurgitation: criteria predictive of death, congestive heart failure and angina in young patients. *Circulation*, **44**, 368.
- TAKEDA, J., WARREN, R. & HOLZMAN, D. (1963) Prognosis of aortic stenosis. Special reference to indications for operative treatment. *Archives of Surgery*, **87**, 931.
- THOMPSON, R., YACOB, M., AHMED, M., SEABRA-GOMES, R., RICKARDS, A. & TOWERS, M. (1979) Influence of pre-operative left ventricular function on results of homograft replacement of the aortic valve for aortic stenosis. *American Journal of Cardiology*, **43**, 929.
- WAGNER, H.R., WEIDMAN, W.H., CURTIS ELLISON, R. & MIETTINEN, O.G. (1977) Indirect assessment of severity in aortic stenosis. *Circulation*, **56** (Suppl.), I-20.
- WOOD, P. (1958) Aortic stenosis. *American Journal of Cardiology*, **1**, 553.