VALVE DISEASE

Interface between valve disease and ischaemic heart disease

Bernard Iung

Cardiology Department, Bichat Hospital, Paris, France

The association of coronary artery disease with heart valve disease is frequently encountered and it can be expected that this association will become more common because of the evolution in the epidemiology of valvar diseases. Degenerative lesions are now the most frequent cause of valve disease in western countries and they frequently occur in old patients, who are also at higher risk for atherosclerotic disease. The association of calcified aortic stenosis and coronary heart disease is the main problem, because it is the most frequently encountered association and because it raises specific questions, particularly in regard to the detection and management of both pathologies. Despite many reports in the literature, recently published guidelines point out the fact that concern remains regarding the optimal strategies for diagnosis and treatment of coronary artery disease in patients with valve disease.[1]

Calcific aortic stenosis associated with coronary artery disease

Frequency of coronary artery disease in patients with calcified aortic stenosis

The frequency of coronary artery disease in patients with calcified aortic stenosis can be correctly assessed only in studies comprising systematic coronary angiography, regardless of the symptoms. The frequency of associated coronary disease varies according to the characteristics of the population involved, in particular age and, to a lesser degree, the geographic origin. Series of patients with calcific aortic stenosis whose mean age is between 60 and 70 years reported 30–50% of associated significant coronary artery disease (at least one stenosis > 50% or 70% of vessel diameter). Coronary artery disease has been reported in more than 50% of patients aged ⩾ 70 years[2] and, of patients aged ⩾ 80 years, in 65% in series from the USA[3] and 41% in a British series.[4]

Series published in the 1960s and '70s led certain authors to suggest that aortic stenosis could have a protective role against coronary atherosclerosis. This was in fact probably only the consequence of a selection bias in series in which the indication of coronary angiography depended on the symptoms. Patients with aortic stenosis and coronary disease became symptomatic earlier in the course of their disease, which could explain the lower incidence and severity of coronary disease than in patients without valve lesions. More recent studies including systematic coronary angiography report frequent association of coronary disease, with a majority of multivessel disease, and therefore do not support this hypothesis of a protective effect.

Calcific aortic stenosis and coronary atherosclerosis were initially considered as two independent diseases, their association being interpreted only as a consequence of their increasing frequency with age. Immunohistochemical analysis of stenotic aortic valves with different levels of severity have shown that early lesions of aortic stenosis have several common features with atherosclerosis, in particular inflammatory cell infiltrates, lipoproteins, and calcium deposits. This is further confirmed by a prospective population based study, in which predictive factors of aortic sclerosis or stenosis were also predictors of atherosclerosis, such as older age, male sex, history of hypertension, smoking, and low density lipoprotein cholesterol.[5] The possibility that calcific aortic stenosis and atherosclerosis could share predisposing factors underlines the importance of assessing coronary status in patients with aortic stenosis.

There are few data regarding the consequence of coronary disease on the adaptation of the left ventricle to aortic stenosis. It seems that patients with coronary disease have a higher systolic wall stress because of a less pronounced hypertrophy, than patients with aortic stenosis and normal coronary arteries.[6] The negative effect of hypertrophy on left ventricular function would therefore appear earlier in the course of aortic stenosis if coronary disease is associated.

Diagnosis of associated coronary stenosis in patients with aortic valve stenosis

Clinical assessment

Angina pectoris has a low positive predictive value of coronary disease in patients with aortic stenosis. Less than 50% of patients with aortic stenosis and typical angina have significant coronary lesions. In the others, myocardial ischaemia can be explained by chronic increased afterload, including increased wall stress, wall thickening, and the modifications in coronary microcirculation encountered in left ventricular hypertrophy. There is no controversy as regards the indications for coronary angiography in patients with aortic stenosis and angina.

On the other hand, the negative predictive value of angina was thought to be high, and some authors in the 1980s recommended not performing coronary angiography in patients with aortic stenosis without angina. However, patients with aortic stenosis can have significant coronary artery stenosis without any chest pain. Left main stenosis or three vessel disease was reported in 14% of the patients with aortic stenosis and no angina.[7]

Non-invasive assessment

Stress tests have been used to detect coronary lesions in patients with aortic valve disease, in particular in conjunction with radionuclide

Correspondence to:
Dr Bernard Iung,
Cardiology
Department, Bichat
Hospital, 46, rue Henri
Huchard, 75018 Paris,
France
email: bernard.iung@
bch.ap-hop-paris.fr

myocardial perfusion imaging using thallium. Such examinations generally have a rather low specificity, because of the possibility of a false positive result related to myocardial hypertrophy. Moreover, sensitivity is < 100%, meaning significant coronary artery disease can be missed. However, the main concern about the use of stress tests on patients with aortic valve stenosis is safety. Stress tests may be performed with specific protocols in patients with asymptomatic aortic stenosis, in order to evaluate their functional capacity accurately. Nevertheless, the presence of symptomatic aortic stenosis remains a contraindication for a stress test in current guidelines. Tests using dipyridamole have the same limitations regarding specificity, sensitivity, and also safety. Stress echocardiography has also been shown to be non-specific of coronary disease in patients with aortic stenosis. The detection of thoracic aortic plaque by transoesophageal echocardiography is a strong predictor of coronary artery disease in patients with aortic stenosis, but 10% of the patients without aortic plaque have significant coronary artery disease. Combined assessment of carotid atherosclerosis using echography could enhance sensitivity, although this remains < 100%. Transoesophageal echocardiography can therefore not be considered as a reliable examination to eliminate associated coronary artery disease. Electron beam computed tomography enables high grade coronary artery stenosis to be detected non-invasively. High sensitivity and specificity have been reported but this examination suffers limitations in availability and feasibility.

Coronary angiography
Given the limitations of non-invasive techniques, the only method for the definite diagnosis of coronary artery disease is coronary angiography. The risk of coronary angiography is very low in patients with aortic stenosis when there is no associated cardiac catheterisation. Echocardiography-Doppler generally allows an accurate evaluation of aortic valve disease and a haemodynamic evaluation is seldom required. North American guidelines recommend performing coronary angiography in patients with heart valve disease where there is chest pain, objective evidence of ischaemia, decreased left ventricular systolic function, history of coronary artery disease or coronary risk factors (including age).[1] The age above which coronary angiography should be systematically performed in the preoperative evaluation of valvar heart disease is difficult to set definitely. North American guidelines recommend coronary angiography in men over 35 years old, in premenopausal women aged over 35 and with coronary risk factors, and in postmenopausal women. A threshold commonly used in Europe is 40 years for men and 50 years for women. With the current predominance of degenerative valve disease, coronary angiography should therefore be considered in nearly all patients with calcific aortic stenosis.

> **Detection of coronary artery disease associated with heart valve disease**
>
> - The sensitivity of stress tests is below 100% and they can therefore miss significant coronary artery disease.
>
> - The main concern of stress tests is their safety in current practice.
>
> - Methods using imaging (transoesophageal echocardiography, electron beam computed tomography) give promising results, but still have limits in feasibility and reliability.
>
> - Coronary angiography is the only current means to ensure a reliable detection of coronary artery disease associated with heart valve disease.
>
> - Coronary angiography should be systematic in preoperative evaluation of heart valve diseases in men aged > 40 years old and women > 50 years old.

Treatment of aortic stenosis associated with coronary arteriosclerosis
It is widely accepted that the treatment for symptomatic aortic stenosis is aortic valve replacement (AVR). Balloon dilatation provides only a limited and transient improvement and does not influence the natural history of the disease. However, concern remains as regards the optimal treatment of aortic stenosis and associated coronary artery disease according to the respective severity of both pathologies.

Symptomatic aortic stenosis associated with significant coronary artery disease
Although the benefits are not irrevocably proven, it is generally accepted that patients with significant aortic stenosis associated with significant coronary artery disease (stenosis > 50% or 70% of vessel diameter) should be treated by combined AVR and coronary artery bypass grafting (CABG).[1] Many series have reported immediate and late results of combined valvar and coronary surgery in patients with aortic and coronary disease and compared these results with those obtained after isolated AVR in patients with aortic stenosis without coronary lesions. It is difficult to summarise the results of all these series, because they are heterogenous in regard to the type of aortic valve disease (aortic stenosis or mixed aortic stenosis and regurgitation), the severity of coronary disease, and the period of operation (table 1).[7–12] Patients treated in the 1980s and '90s were older and had more frequent coronary diseases.[2] This evolution may explain the persistence of a relatively high operative mortality of combined AVR and CABG, between 5–10% in most series. The improvement of perioperative management is probably partly counterbalanced by the increasing proportion of elderly patients with comorbidities.

Comparative studies most often reported higher perioperative mortality rates after com-

348

bined surgery than after AVR alone. The relevance of such comparisons is, however, limited by the fact that patients with or without coronary artery disease differ by many characteristics. In particular, patients with coronary artery disease are generally older, more symptomatic, and more frequently have left ventricular dysfunction. We attempted to diminish the effect of these confounding factors in a study comparing patients undergoing combined aortic and coronary surgery with patients having normal coronary arteries and undergoing isolated AVR, who were matched for age, sex, functional class, left ventricular ejection fraction, and the date of operation.[11] Despite matching in some important predictive factors, there remained a trend towards a higher operative mortality (10.4% *v* 4.9%, p = 0.08) in patients undergoing combined aortic and coronary surgery. In multivariate analysis taking into account other patient characteristics, combined CABG is associated with a lower increase in operative mortality than in univariate analysis.[2] These findings do not indicate that CABG in itself increases the risk of AVR, but should be interpreted as the adverse influence of an associated atherosclerotic disease on the result of cardiac surgery.

Long term results after AVR associated with CABG are generally good, with survival rates > 60% at nine and 10 years in recent studies, despite the high risk profile of the patients (table 1).[10 11] The comparison of late results after isolated AVR in patients with normal coronary arteries reveals the same limitations as the comparison of early mortality, because of the differences in the patients involved. In matched populations, mortality was not significantly higher in patients undergoing combined surgery up to nine years after the postoperative period.[11] Relative survival, compared with a standard population, was not influenced by CABG until 10 years after surgery in another series.[2] Apart from survival, late functional results are excellent in most series, most patients being in New York Heart Association (NYHA) class I–II, without a low incidence of angina and acute coronary events.[9–11]

Despite a trend towards an increase in perioperative mortality compared with patients with normal coronary arteries, the immediate results of AVR associated with CABG are satisfying according to the characteristics of the patients involved. These results support the current practice which is to bypass significant coronary artery stenosis (50% for left main and 50–70% for other arteries) when possible in

Figure 1. Calcified aortic stenosis associated with a 50% distal left main stem stenosis.
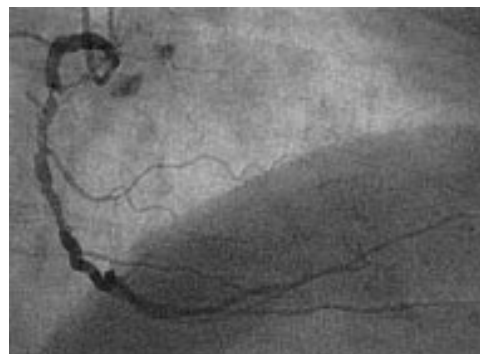

Figure 2. Calcified aortic stenosis with a tight stenosis on the second segment of a diffusely atherosclerotic right coronary artery.

patients who should have AVR for aortic valve stenosis (figs 1 and 2).[1] The extrapolation of large series on CABG suggests that the use of the left internal mammary artery should be recommended for the grafting of the left anterior descending artery in those patients more frequently operated on at an advanced age, and for whom late reoperation should be avoided.

Isolated AVR in patients with coronary artery stenosis

Published series comprise only a few patients who had coronary stenosis associated with aortic stenosis and who underwent isolated AVR without CABG. Moreover, these patients constitute a particularly heterogeneous group, because the absence of CABG can be related to very different situations, whether it is deliberate in moderate stenosis (approximately 50%) or impossible in significant stenosis because of anatomical conditions. The absence of CABG was deliberate in all cases only in the Bonow series,[13] which reported a favourable outcome but whose interpretation should take into

Table 1 Results of aortic valve replacement combined with coronary artery bypass grafting in patients with aortic valve disease associated with coronary artery disease

Series	Years of operation	AVR+ CABG (n)	AS (n)	Mean age (years)	3 vessel or LM (%)	Operative deaths (%)	Late survival (%)
Mullany[7]	1967–76	112	–	–	34	6.3	49 at 10 years
	1982–83	99	–	–	48	4.01	
Lytle[8]	1967–91	500	–	62	23	5.8	52 at 10 years*
Czer[9]	1969–84	233	–	67	52	8.2	41 at 10 years
Lund[10]	1975–86	–	55	64	47	3.6	62 at 10 years
Iung[11]	1979–92	–	144	69	31	10.4	67 at 9 years
Flameng[12]	1980–92	449	–	65	30	7.6	–

*Among postoperative survivors.
AVR, aortic valve replacement; AS, aortic stenosis; CABG, coronary artery bypass grafting, LM, left main stenosis.

350

Figure 3. Calcified aortic stenosis with atherosclerosis of left anterior descending and circumflex arteries, no stenosis being more than 50%.

account the majority of mono-vessel diseases and the short follow up. In our experience, mid term outcome after isolated AVR in patients who had aortic stenosis associated with moderate coronary artery stenosis (40–60%) is excellent and identical to patients with normal coronary arteries (fig 3).[11] As regards patients who had aortic stenosis and significant coronary disease which could not be bypassed for technical reasons, there was a trend towards a higher postoperative mortality and a more rapid decrease of the survival curve after a four year follow up.[7 10 11] However, mid term survival was satisfying (60% at five years) and functional results were good, with more than 90% of the patients being free from angina in the absence of CABG.[11] It is necessary to be cautious given the small number of patients, but these results strongly suggest that AVR should be performed in patients with symptomatic aortic stenosis, even if they have significant coronary lesions which cannot be bypassed for technical reasons. Immediate and late results seem less satisfying than those in patients who underwent combined aortic and coronary surgery but are far better than the natural history of aortic stenosis. Future studies are needed to evaluate the association of transmyocardial laser revascularisation with AVR in such patients.

Moderate aortic stenosis associated with significant coronary artery disease
In patients who have moderate aortic stenosis and significant coronary artery disease for which there is an indication for revascularisation, percutaneous coronary angioplasty should be considered if possible. In patients who have coronary artery disease requiring CABG, the therapeutic choice is between :
- associating AVR and CABG, which is a radical treatment but exposes the patient to a higher operative risk and, later, to prosthetic related complications;
- performing only CABG, which will expose the patient to a subsequent AVR in case of progression of the aortic stenosis.
The mean rate of progression of aortic stenosis has been estimated at between 5–8 mm Hg per year for mean gradient, with a mean decline between 0.1–0.2 cm^2 per year in valve area.[14] However, it is very difficult to predict the progression of aortic stenosis in any given patient. Valve replacement in a patient who has previously undergone CABG can be technically complex and associated with an increased mortality.[15] The possible evolution of moderate aortic stenosis and the risk of subsequent surgery leads to AVR, associated with CABG, being recommended in patients who have moderate aortic stenosis associated with coronary lesions requiring surgery. Valve replacement should be performed if valve area is below 1 cm^2 and considered if between 1–1.5 cm^2, and/or if mean aortic gradient is between 30–50 mm Hg.[1]

Choice of prosthesis
The major determinant of the choice between a mechanical prosthesis and a bioprosthesis is the comparison between the presumed life expectancy of the patient and the duration of the prosthesis. Bioprostheses are clearly recommended for patients over 80 years old, while mechanical prostheses are generally preferred in patients aged < 70 years. The choice may be difficult between 70 and 80 years. Coronary disease is frequently associated in this age group and can be considered as a promoting factor for a mechanical prosthesis, though this point is controversial.[16] Patients undergoing combined aortic and coronary surgery may have a life expectancy that will expose them to primary degeneration of the bioprosthesis. The risk of reoperation, which is still high in the elderly, is even more increased in patients who have previously undergone combined aortic and coronary surgery.

Medical treatment after combined aortic and coronary surgery
Patients who have undergone AVR with a mechanical prosthesis can benefit from moderate anticoagulation (target international normalised ratio 2–3), provided their thromboembolic risk is low—that is, patients in sinus rhythm, without previous embolism and with no severe enlargement of the left atrium.[17] Moderate anticoagulation ensures an efficient protection against embolic events at a lower haemorrhagic risk. This point is particularly important after combined aortic and coronary surgery because patients should also be treated with aspirin. The combination of anticoagulants and aspirin is not recommended in all patients with prosthetic heart valves, but its use is supported by the results of clinical trials in patients who have mechanical heart valves associated with atherosclerotic disease.

Patients with CABG particularly benefit from treatment with statins. It is logical to consider prescribing a statin in most, if not all, patients who have undergone combined aortic and coronary surgery. The choice of the type of statin must take into account the possibility of drug interaction with oral anticoagulant treatment.

Combined aortic valve replacement and coronary artery bypass grafting (CABG)

● CABG should be conducted in association with aortic valve replacement, when possible, for all coronary arteries with significant stenosis.

● In patients who have significant, non-bypassable coronary artery stenosis, aortic valve replacement, if otherwise indicated, should not be contraindicated on the basis of coronary status.

● The progression of aortic stenosis and the problems related to valve replacement after previous coronary surgery support wide indications for aortic valve replacement in patients who have moderate aortic stenosis and in whom CABG is indicated.

Coronary artery disease associated with other valve diseases

Aortic regurgitation

Left ventricular ejection fraction is clearly an important parameter to be taken into account in the decision to operate on a patient with severe aortic regurgitation, particularly in the absence of symptoms. In the case of significant coronary artery disease, the respective roles of aortic regurgitation and coronary disease in ventricular dysfunction can be debated. However, there are no grounds for using different thresholds in patients with or without coronary artery disease.

Just as in other valve diseases, degenerative lesions are a growing cause of aortic regurgitation. Degenerative aortic regurgitation may be associated with an aneurysm of the ascending aorta, thereby requiring not only valve replacement but a composite replacement with an aortic tube and a prosthesis associated with reimplantation of the coronary arteries. If the patient also requires CABG, mammary artery grafts should be used if possible to avoid the anastomosis of the grafts on the pathological ascending thoracic aorta.

Mitral stenosis

The frequency of coronary artery disease is low among patients with mitral stenosis because this rheumatic disease is predominantly found in young patients. In older patients the diagnosis and therapeutic management of coronary artery disease does not differ from other valve diseases. Angina pectoris can occur in patients with mitral stenosis and normal coronary arteries, and it could be related to ischaemia of the right ventricle. The only other unique feature of coronary disease in patients with mitral stenosis is the possibility of coronary embolism.

Mitral regurgitation

The association of mitral regurgitation and coronary artery disease differs from the association of other valve diseases with coronary atherosclerosis. As in other cases, this can be the conjunction of two different pathologies, but also a unique pathology, coronary artery disease being the only cause in the case of ischaemic mitral regurgitation.

Coronary artery disease associated with non-ischaemic mitral regurgitation
On this topic there are less data in the literature, compared with the association of aortic valve and coronary diseases, and most series concern mitral valve replacement associated with CABG. Combined valvar and coronary surgery is associated with a trend towards a higher perioperative mortality, but patients with associated coronary artery disease are also at higher risk than patients with isolated mitral valve disease and normal coronary arteries.[18 19]

However, with the evolution of the epidemiology of heart valve disease and the improvement in techniques of valve repair, combined surgery performed in patients with mitral regurgitation in western countries most frequently associates mitral valve repair and CABG. The advantages of valve repair over valve replacement—that is, lower perioperative mortality and improved event-free late outcome—should be taken into account when associating valve repair with CABG, particularly in patients who have a preoperative impairment of left ventricular function. The advantages of an early operation in patients with severe mitral regurgitation are even more pronounced in patients who have concomitant coronary artery disease.[20] The association of coronary lesions with severe mitral regurgitation should therefore be an incentive to consider an early valve repair.

Ischaemic mitral regurgitation
Tackling the subject of mitral regurgitation in depth is beyond the scope of this paper, because it should not be considered as an interface between valvar and coronary disease, but only as an ischaemic disease.

Acute ischaemic mitral regurgitation is caused by rupture of the papillary muscle occurring at the acute phase of myocardial infarction, generally with an inferior location. Despite the high risk, urgent surgery is mandatory because of the catastrophic prognosis.

Most problems in managing ischaemic mitral regurgitation are encountered in patients with chronic ischaemic mitral regurgitation. Such patients have normal leaflets and the regurgitation is caused by modifications of the geometry and kinetics of the subvalvar apparatus, as a consequence of the abnormalities of local myocardial contraction. Quantification of the regurgitation may be difficult, particularly because of the possibility of variations in the grade of mitral regurgitation according to the ischaemia.

There is a consensus for performing combined mitral and coronary surgery in the case of severe ischaemic mitral regurgitation (grade 3 or 4), although the operative risk is generally higher than in the case of non-ischaemic mitral regurgitation associated with coronary disease.

351

352

> **Mitral regurgitation associated with coronary artery disease**
>
> - The mechanism of mitral regurgitation should be carefully assessed in the preoperative evaluation:
>   – to differentiate ischaemic mitral regurgitation from non-ischaemic regurgitation associated with coronary disease;
>   – to evaluate the possibility of valve repair.
>
> - Valve repair should be considered early—that is, in NYHA class I or II—in patients who have severe mitral regurgitation associated with coronary artery disease.

Valve repair gives good immediate and mid term results in such patients, but we only have a few series with limited follow up.

The treatment of moderate ischaemic mitral regurgitation (grade 2) is a matter of debate. Moderate regurgitation is traditionally not corrected at the time of CABG. However, a subgroup analysis of the SAVE (survival and ventricular enlargement) study suggests that moderate mitral regurgitation has a negative prognostic value on the outcome of patients following myocardial infarction. Whether the correction of moderate ischaemic mitral regurgitation by valve repair will improve the outcome of such patients remains to be determined by further studies.

1. **ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease.** A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *J Am Coll Cardiol* 1998;**32**:1486–88.
- *These recent guidelines summarise most aspects of the management of valvar diseases, in particular as regards paraclinic assessment and indications for surgery. Recommendations are given regarding indications for coronary angiography in patients with valvar disease and for aortic valve replacement in patients undergoing coronary surgery.*

2. **Kvidal P, Bergström R, Hörte LG,** *et al.* Observed and relative survival after aortic valve replacement. *J Am Coll Cardiol* 2000;**35**:747–56.
- *This large series with a long term follow up is particularly interesting owing to its analysis not only of absolute survival, but also relative survival as compared with a standard population. This provides useful information on predictive factors of late results of aortic valve replacement, in particular in patients aged over 70 years.*

3. **Akins CW, Daggett WM, Vlahakes GJ,** *et al.* Cardiac operations in patients 80 years old and older. *Ann Thorac Surg* 1997;**64**:606–15.

4. **Gilbert T, Orr W, Banning AP.** Surgery for aortic stenosis in severely symptomatic patients older than 80 years: experience in a single UK centre. *Heart* 1999;**82**:138–42.

5. **Stewart BF, Siscovick D, Lind BK,** *et al.* Clinical factors associated with calcific aortic valve disease. Cardiovascular health study. *J Am Coll Cardiol* 1997;**29**:630–4.
- *A large population based study which enables the frequency of different degrees of aortic stenosis to be assessed. The analysis of predictive factors suggests the possibility of common factors in the pathogenesis of atherosclerosis and degenerative aortic stenosis.*

6. **Lund O, Flo C, Jensen FT,** *et al.* Left ventricular systolic and diastolic function in aortic stenosis. Prognostic value after valve replacement and underlying mechanisms. *Eur Heart J* 1997;**18**:1977–87.

7. **Mullany CJ, Elveback LR, Frye RL,** *et al.* Coronary artery disease and its management: influence on survival in patients undergoing aortic valve replacement. *J Am Coll Cardiol* 1987;**10**: 66–72.
- *A comparative study of patients undergoing isolated aortic valve replacement with or without coronary disease and patients undergoing combined aortic and coronary surgery over two time periods. The results support a wide use of preoperative coronary angiography and the association of bypass grafting with aortic valve replacement.*

8. **Lytle BW, Cosgrove DM, Gill CC.** Aortic valve replacement combined with myocardial revascularization. *J Thorac Cardiovasc Surg* 1988;**95**:402–14.
- *A study of 500 patients treated by combined aortic valve replacement and coronary surgery, with a 10 year follow up and an analysis of the predictive factors of late results.*

9. **Czer LS, Gray RJ, Stewart ME,** *et al.* Reduction in sudden late death by concomitant revascularization with aortic valve replacement. *J Thorac Cardiovasc Surg* 1988;**95**:390–401.
- *This comparative study comprises 474 patients operated on for aortic valve replacement with or without bypass grafting. Despite differences in patient characteristics, long term results (up to 12 years) suggest a benefit of associating coronary and aortic surgery.*

10. **Lund O, Nielsen TT, Pilegaard HK,** *et al.* The influence of coronary artery disease and bypass grafting on early and late survival after valve replacement for aortic stenosis. *J Thorac Cardiovasc Surg* 1990;**100**:327–37.

11. **Iung B, Drissi MF, Michel PL,** *et al.* Prognosis of valve replacement for aortic stenosis with or without coexisting coronary heart disease: a comparative study. *J Heart Valve Dis* 1993;**2**:259–266.
- *This study compared 144 patients treated by combined aortic and coronary surgery with 144 other patients operated on for aortic stenosis with normal coronary arteries, and who were matched for the main predictors of immediate and late results. There is a trend toward a higher operative mortality but not towards late death in the patients who had combined surgery.*

12. **Flameng WJ, Herijgers P, Szecsi J,** *et al.* Determinants of early and late results of combined valve operations and coronary artery bypass grafting. *Ann Thorac Surg* 1996;**61**:621–8.

13. **Bonow RO, Kent KM, Rosing D,** *et al.* Aortic valve replacement without myocardial revascularization in patients with combined aortic valvular and coronary artery disease. *Circulation* 1981;**63**:243–51.
- *This comparative study reports good results of isolated aortic valve replacement in patients with aortic stenosis and coronary artery disease. However, the low severity of coronary lesions (18% of three vessel disease) and the follow up of only four years limit the relevance of the findings.*

14. **Brener SJ, Duffy CI, Thomas JD,** *et al.* Progression of aortic stenosis in 394 patients: relation to changes in myocardial and mitral valve dysfunction. *J Am Coll Cardiol* 1995,**25**:305–10.

15. **Odell JA, Mullany CJ, Schaff HV,** *et al.* Aortic valve replacement after previous coronary artery bypass grafting. *Ann Thorac Surg* 1996;**62**:1424–30.
- *This series includes 145 patients operated on for aortic valve replacement after a previous coronary bypass grafting. It shows an increased operative morbidity and mortality, and generally recommends valve replacement in patients with moderate aortic stenosis who need coronary surgery.*

16. **Jones EL, Weintraub WS, Craver JM,** *et al.* Interaction of age and coronary disease after valve replacement: implications for valve selection. *Ann Thorac Surg* 1994;**58**:378–85.

17. **Acar J, Iung B, Boissel JP,** *et al.* AREVA: multicenter randomized comparison of low-dose vs. standard dose anticoagulation in patients with mechanical prosthetic heart valves. *Circulation* 1996;**94**:2107–12.
- *This prospective, randomised trial concludes that there is a benefit from using moderate anticoagulation in selected patients after aortic valve replacement with a mechanical prosthesis. This is associated with a lower rate of bleeding without increasing the thromboembolic risk.*

18. **Lytle BW, Cosgrove DM, Gill CC,** *et al.* Mitral valve replacement combined with myocardial revascularization: early and late results for 300 patients, 1970 to 1983. *Circulation* 1985;**71**:1179–90.

19. **He GW, Hughes CF, McCaughan B,** *et al.* Mitral valve replacement combined with coronary artery operation: determinants of early and late results. *Ann Thorac Surg* 1991;**51**:916–23.

20. **Triboulloy C, Enriquez-Sarano M, Schaff HV,** *et al.* Impact of preoperative symptoms on survival after surgical correction of organic mitral regurgitation. Rationale for optimizing surgical indications. *Circulation* 1999;**99**:400–5.

website extra

Additional references appear on the Heart website

www.heartjnl.com