Clinical Perspective

Should early elective surgery be performed in patients with severe but asymptomatic aortic stenosis?

Introduction

It has been well known for many years that symptomatic patients with severe aortic stenosis have a very poor outcome. Average survival after the onset of symptoms has been reported to be less than 2 to 3 years[1–10]. In this situation, valve replacement not only results in dramatic symptomatic improvement but also in good long-term survival[2,11–16]. This holds true even for patients with already reduced left ventricular function, as long as functional impairment is caused by aortic stenosis[12,16]. There is general agreement that, in the absence of serious co-morbidity, surgery must be strongly recommended for patients with severe aortic stenosis who develop symptoms of congestive heart failure, exertional angina and dizziness or syncope during exercise.

In contrast, the management of asymptomatic patients with severe aortic stenosis remains a matter of controversy[17]. Many cardiologists are reluctant to send asymptomatic patients for surgery[18] while others are concerned about following these patients conservatively.

Because of the widespread use of Doppler echocardiography and because aortic valve replacement is offered regardless of age, cardiologists are increasingly faced with the difficult decision of whether to operate on these patients or not.

Arguments in favour of early elective surgery

Risk of sudden cardiac death

When following asymptomatic patients with aortic stenosis conservatively, sudden death is probably the major concern. Prospective data in this respect are still limited. In three studies where significant numbers of patients with non-severe stenosis were included, no sudden death was reported: Otto et al.[19] followed 123 patients with an average peak velocity of 3·6 ± 0·6 m·s⁻¹ for 30 months. The two other series with 51[6] and 37 patients[20] had follow-up periods of 1·5 and 2·0 years, respectively. Only two studies reported the outcome of larger cohorts of patients with exclusively severe stenosis as defined by a peak aortic jet velocity ≥4·0 m·s⁻¹. Pellikka et al.[21] observed two sudden deaths among 113 patients during a mean follow-up of 20 months. Both patients, however, had developed symptoms at least 3 months before death. Rosenhek et al.[22] reported one sudden death that was not preceded by any symptoms among 104 patients followed for 27 months on average. Thus, sudden death may indeed occur even in the absence of preceding symptoms in patients with aortic stenosis, but this appears to be a very uncommon event, with a rate of probably less than 1% per year during the asymptomatic phase of the disease. Finally, it has to be considered, that sudden death has even been reported after successful valve replacement and that therefore this risk cannot be entirely eliminated by surgical treatment[23,24].

Risk of death between onset of symptoms and surgical treatment

The fact that patients do not always promptly report their symptoms while at high risk of abrupt deterioration and sudden death is an important concern. For example, Pellikka and co-workers[21] lost two patients from sudden death who were retrospectively found to have developed symptoms over recent months. Despite proper education, not all patients will seek immediate medical help with the first onset of symptoms.

In addition, it has to be considered that, at least in some countries, patients may wait several months for surgery. In a Scandinavian study, for example, seven of 99 patients with severe aortic stenosis who were

Revision submitted 31 December 2001 and accepted 2 January 2002.

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scheduled for surgery died during an average waiting period of 6 months\[^{23}\].

**Risk of developing irreversible myocardial damage**

In contrast to valvular regurgitation, patients with asymptomatic severe aortic stenosis who have already developed impaired systolic left ventricular function are extremely uncommon. There is speculation that myocardial fibrosis and severe left ventricular hypertrophy, that may not be reversible after delayed surgery, could preclude an optimal postoperative outcome. However, there are, so far, no data to support this hypothesis. Considering the excellent outcome after valve replacement in isolated aortic stenosis with normal systolic left ventricular function, it is unlikely that the risk of developing irreversible myocardial damage will play a major role.

**Rapid development of symptoms**

Some studies reported a very poor outcome with up to 80\% of the patients requiring valve replacement within 2 years\[^{19}\]. Such observations have also raised the question as to whether it is worthwhile delaying surgery in patients who are still asymptomatic. However, other investigators have reported better outcome, and individual outcome varies widely. For example, survival free of death or valve replacement indicated by the development of symptoms was 56 ± 5\% at 2 years in the series reported by Rosenhek et al.\[^{22}\]. These discrepant results may be explained by the fact that in some studies patients underwent surgery without having developed symptoms while these interventions were, nevertheless, counted as events. Thus, the event-free survival reported in the literature has to be viewed with caution.

**Increased operative risk in severely symptomatic patients**

Patients with severe symptoms have been found to have a significantly higher operative mortality than those with no or only mild symptoms. According to the STS U.S. cardiac surgery database 1997, patients in NYHA classes I or II had an operative mortality of less than 2\% compared with 3·7\% and 7·0\% for patients in NYHA class III and IV, respectively\[^{26}\]. In addition, urgent or emergency valve replacement carries a significantly higher risk than elective surgery\[^{26}\].

**Arguments against early elective surgery**

**Operative risk**

Although the operative risk has dramatically decreased in recent decades it must be considered to be in the range of at least 2 to 3\%\[^{11,26}\]. Operative mortality may be as high as 10\% in the elderly\[^{27}\] and even markedly higher in the presence of co-morbidities such as coronary artery disease\[^{28}\]. In an asymptomatic patient this risk has to be outweighed by a proven benefit.

**Prosthetic valve related long-term morbidity and mortality**

After valve replacement with a mechanical or bioprosthetic valve, valve related complications such as thromboembolism, bleeding, endocarditis, valve thrombosis, paravalvular regurgitation and valve failure occur at the rate of at least 2 to 3\% per year. Death directly related to the prosthesis has been reported at a rate of up to 1\% per year\[^{17}\].

**Individual variation of outcome**

The individual course of the disease is highly variable and some patients have been followed for many years without developing symptoms. As valve replacement does not represent a cure in this disease, a general recommendation of early surgery cannot, therefore, be justified.

Thus, the decision over valve replacement in asymptomatic patients remains difficult. Waiting too long may put the patient at an increased risk of sudden death and higher operative mortality whereas operating on a patient too early puts him at an anticipated operative risk and risk of prosthetic-valve related complications. Thus, predictors of outcome that help us to identify high-risk patients who are likely to benefit from early elective surgery are needed.

**Predictors of outcome in asymptomatic, severe aortic stenosis**

**Clinical predictors of outcome**

Several clinical variables have been evaluated with respect to their value as predictors of outcome. However, age, gender, hypertension, hypercholesterolaemia, diabetes mellitus, left ventricular hypertrophy, ventricular ectopic activity, coronary artery disease,
cigarette smoking, use of digoxin, use of a diuretic drug, and the cause of aortic stenosis were found not to be independent predictors and may not be helpful in selecting asymptomatic patients for surgery\cite{19,21,22}.

**Echocardiographic predictors of outcome**

Among the echocardiographic parameters, peak aortic jet velocity and ejection fraction\cite{21} as well as the rate of haemodynamic progression\cite{19} were identified as independent predictors of outcome. However, these findings were obtained retrospectively and did not allow any specific recommendations on how to prospectively select high-risk patients who may benefit from early elective surgery. Quantification of aortic stenosis and the definition of haemodynamically severe stenosis may be problematic. Although there is no general agreement, a cut-off value of 4 m s\(^{-1}\) for the peak aortic jet velocity (corresponding to a peak gradient of 64 mmHg) and/or an aortic valve area of less than 1-0 cm\(^2\) has been used in recent studies to define severe aortic stenosis\cite{19,21,22}. For individual decision making, however, body size and weight should be considered when using such cut-off values.

In a more recent study\cite{22}, aortic valve calcification turned out to be a powerful independent predictor of outcome. Event-free survival at 4 years was 75 \pm 9\% in patients with no or only mild calcification vs 20 \pm 5\% in those with moderately or severely calcified valves. The worse outcome of patients with more severe calcification appeared to be paralleled by more rapid haemodynamic progression. However, even in the presence of calcification the rate of haemodynamic progression varies widely\cite{29,30}. In fact, haemodynamic progression, as determined by serial echocardiographic examination, appears to yield important prognostic information in addition to the degree of calcification. The combination of a calcified valve with a rapid increase in velocity of \(\geq 0.3 \text{ m s}^{-1}\) from one visit to the next within 1 year has been shown to identify a high risk group of patients. Approximately 80\% of them required surgery or died within 2 years\cite{22}.

**Exercise test**

Although Otto et al.\cite{19} reported in their group of asymptomatic patients with aortic stenosis, that those with an end point had a smaller exercise increase in valve area, blood pressure and cardiac output, none of these variables were independent predictors of outcome by multivariate analysis. Amato et al.\cite{31} recently suggested that exercise testing may provide helpful information in the selection of high risk patients, but more data are needed for final conclusions. Nevertheless, exercise testing has been shown to be helpful for the evaluation of reportedly asymptomatic patients. Das et al.\cite{32} recently reported that 36\% of 58 consecutive patients with aortic stenosis, who had denied symptoms, experienced significant symptoms during exercise testing. In addition, despite the lack of solid evidence, most physicians believe that an abnormal haemodynamic response to exercise (e.g. hypotension) in a patient with severe aortic stenosis is a sufficient reason to consider surgery\cite{17}. It has to be emphasized that exercise testing is only appropriate in asymptomatic patients and should definitely not be performed in symptomatic patients. When properly performed, exercise testing in asymptomatic patients with severe aortic stenosis has been shown to be safe\cite{31}.

**Current practice guidelines for the management of asymptomatic patients with severe aortic stenosis and clinical impact of recently identified predictors of outcome**

Based on the data showing that it is relatively safe to delay surgery until symptoms develop, current AHA/ACC practice guidelines definitely recommend aortic valve replacement only in symptomatic patients with severe aortic stenosis and in those asymptomatic patients who undergo cardiac surgery for any other reason such as coronary artery bypass surgery, surgery of the aorta or other heart valves (Class I)\cite{17}.

Although controversial, weight of evidence/opinion is considered in favour of surgery (class IIa) in asymptomatic patients with severe aortic stenosis who present with impaired systolic left ventricular function and in patients with an abnormal response to exercise (e.g. hypotension).

Ventricular tachycardia, marked or excessive left ventricular hypertrophy (15 mm) and a valve area <0.6 cm\(^2\) are less well established as indications for surgery and are thus considered class IIb indications.

Taking into account more recent findings, we would suggest expanding the recommendations for asymptomatic severe aortic stenosis by using echocardiography for risk stratification in the following way\cite{22}.

Patients with no or only mild calcification of their stenotic aortic valve represent a group with a low likelihood of developing symptoms and requiring surgery in the near future. They may remain asymptomatic for many years. Annual follow-up visits and the advice to promptly report the development of any

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Eur Heart J, Vol. 23, issue 18, September 2002
exertional chest pain, dyspnea or lightheadedness at exercise appears to be appropriate for these patients. Patients with moderately or severely calcified valves represent a group with significantly worse outcome. Rapid progression must be expected and a closer follow-up is required.

Patients with moderately or severely calcified valves in whom serial echocardiographic testing reveals rapid progression with a steep increase in jet velocity ($\geq 0.3 \text{ m.s}^{-1} \text{ year}^{-1}$) identifies a high risk patient group. As patients do not always promptly report the development of symptoms and since there is risk of death on the waiting list for surgery, and higher operative risk in severely symptomatic patients, it may be worthwhile considering elective valve replacement instead of waiting for symptoms in this high risk group.

**Considerations in specific patient subgroups**

There is general agreement, that patients with severe asymptomatic aortic stenosis who undergo other cardiac surgery, such as coronary artery bypass grafting, surgery of other valves or the aorta should have aortic valve replacement at the same time\[17\].

In patients with severe asymptomatic aortic stenosis undergoing non-cardiac surgery the risks of the procedures have to be carefully weighed.

Finally, in young patients who plan to become pregnant, aortic valveplasty must be strongly considered.

In addition to these considerations, it has to be emphasized that the decision of performing valve replacement must be individualized, taking into account the patients risk profile and willingness to undergo surgery.

**Conclusion**

Currently available data suggest that careful weighing of risk and benefit does not justify the general recommendation of early elective surgery in asymptomatic patients with severe aortic stenosis. Echocardiographic assessment of the extent of valve calcification and of haemodynamic progression appears to be helpful for risk stratification. Future studies must focus on the identification of additional predictors of outcome to expand our knowledge on how to optimally select patients at risk who may benefit from early elective surgery.

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**References**


