Long-term relative survival after primary heart valve replacement

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Abstract

Objective: Determination of the optimal timing of primary heart valve replacement is an important issue. The present paper provides a synopsis over early and late survival after primary heart valve replacement, including an evaluation of the excess mortality among heart valve replacement patients compared with the general population.

Methods: Survival was analyzed in 2365 patients (1568 without and 797 with concomitant coronary artery bypass grafting (CABG)) who underwent their first heart valve replacement. Observed survival was related to that expected among persons from the general Swedish population stratified by age, sex, and 5-year calendar period, to calculate the relative survival and estimate the disease-specific survival.

Results: Early mortality (death within 30 days after surgery) was 5.9% after aortic valve replacement, 10.4% after mitral valve replacement and 10.6% after combined aortic and mitral valve replacement. Relative survival rates (excluding early deaths) were 84% 10 years after aortic, 68.5% after mitral and 80.9% after both aortic and mitral valve replacement. A multivariate model based on observed survival rates was produced for each group, using the Cox proportional hazards model. Concomitant CABG, advanced New York Heart Association (NYHA) class, preoperative atrial fibrillation, pure aortic regurgitation and higher age increased the late observed survival after aortic valve replacement. Relative survival rates (excluding early deaths) were 84% 10 years after aortic, 68.5% after mitral and 80.9% after both aortic and mitral valve replacement. A multivariate model based on observed survival rates was produced for each group, using the Cox proportional hazards model. Concomitant CABG, advanced New York Heart Association (NYHA) class, preoperative atrial fibrillation, pure aortic regurgitation and higher age increased the late observed survival after aortic valve replacement. NYHA class was the only factor independently related to observed late deaths after mitral valve replacement, and mitral insufficiency the only corresponding factor after both aortic and mitral valve surgery.

Conclusion: The use of relative survival rates tended to modify the difference between subgroups compared with observed survival rates. Relative survival rates reduced the effect of concomitant CABG on survival, but enhanced for example the effect of aortic regurgitation. In patients ≥ 70 years of age and patients submitted to aortic or mitral valve replacement with mild or no symptoms, the survival rate was similar for many years to that in the Swedish population at large.

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Keywords: Heart valve replacement; Relative survival; Survival

1. Introduction

The present study provides an overview of early and late crude survival and late relative survival after primary heart valve replacement among all patients undergoing this operation in Uppsala, Sweden, during a 12-year period. Relative survival is a measure of the excess mortality among heart valve replacement patients compared with the general population. In particular we studied the excess mortality in certain subgroups in order to shed some light on the question as to the optimal timing of surgery [14].

To obtain the relative survival in our study group of 2365 patients, we compared the survival rate in these patients with that in the total Swedish population, adjusted for sex, age and 5-year calendar period.

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2. Methods

2.1. Patients

Between January 1980 and June 1992, 2365 patients underwent primary heart valve replacement with (797) or without (1568) concomitant coronary artery bypass grafting (CABG), at the Department of Thoracic and Cardiovascular Surgery of the University Hospital, Uppsala, Sweden.

There were 1380 men (58%) (mean age 61.8 years, range 19.5–84) and 985 women (42%) (mean age 64.7 years, range 19–85). Preoperative coronary angiography was performed in all patients aged 50 years or more and all patients with angina or in whom coronary artery disease (CAD) could be suspected on a clinical basis.

Aortic valve replacement (AVR) was carried out in 1658 patients, including 585 patients (35%) who also underwent CABG, and mitral valve replacement (MVR) in 500 patients, including 166 (33%) with concomitant CABG. Both aortic and mitral valve replacement was undertaken in 207 patients (double valve replacement, DVR group), of whom 35 (17%) also had CABG. Clinical data for all patients are given in Table 1.

All operations were performed with a standard technique for cardiopulmonary bypass and moderate hypothermia (25–32°C). Singledose or multidose cold crystalloid cardioplegic solution (modified St. Thomas) was the most frequently applied method. A small number of patients had cold blood cardioplegia.

Our current policy is to recommend a bioprosthesis to patients aged 70 years or more. However, the type and trade-mark of the prosthesis was left to the discretion

Table 2

<table>
<thead>
<tr>
<th>Causes of early death</th>
<th>Valve replacement group</th>
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<tr>
<td></td>
<td>Aortic</td>
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<tr>
<td>Primary cardiac</td>
<td>60</td>
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<tr>
<td>Prosthesis dysfunction</td>
<td>2</td>
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<tr>
<td>Pulmonary embolism</td>
<td>3</td>
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<td>Sudden death</td>
<td>3</td>
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<tr>
<td>Neurological damage</td>
<td>5</td>
</tr>
<tr>
<td>Multiple organ failure</td>
<td>16</td>
</tr>
<tr>
<td>Severe bleeding</td>
<td>6</td>
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<tr>
<td>Infection</td>
<td>3</td>
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<tr>
<td>Other</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
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of each surgeon. In the AVR group, 1337 received a mechanical valve (St Jude 194, BjörkShiley 614, Duromedic 199, Carbomedic 100 and composite graft 5) and 321 patients a bioprosthesis (Carpentier-Edwards 101, Sorin 107, St Jude bioprosthesis 32 and miscellaneous types 81). In the MVR group 439 had a mechanical valve (St Jude 188, BjörkShiley 187, Duromedic 62 and Carbomedic 2) and 61 a bioprosthesis (Carpentier-Edwards 9, Sorin 4, miscellaneous types 48). In the DVR group, 184 patients had a mechanical valve (St Jude 61, BjörkShiley 94, Duromedic 22 and Carbomedic 7) and 23 a bioprosthesis (Carpentier-Edwards 4, Sorin 4, miscellaneous types 15). Five patients in the AVR-group had concomitant mitral annuloplasty, 14 in the MVR group and 6 in the DVR group had concomitant tricuspid annuloplasty.

Oral anticoagulants were recommended. Patients with a mechanical valve were prescribed life-long treatment, while most patients with a bioprosthesis were recommended three months of anticoagulatia, unless atrial fibrillation or other conditions indicated a high risk of thromboembolism. The therapeutic level of prothrombin complex (factors II, VII and X) ranges from 15–25%, corresponding to the INR of 1.9–2.8.

2.2. Data collection, follow-up and outcome events

All clinical data were recorded prospectively and stored in a computer.

A unique 10-digit national registration number is allocated to every Swedish citizen. In January 1993 all patients were followed up with respect to survival by computerized linkage to two national registers, namely

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Fig. 1. Observed (— ● —) and relative (— ○ —) survival after primary aortic valve replacement in patients who survived the first postoperative month; n = 1560. 95% confidence intervals at 5 and 10 years and the number (N) of patients at risk are given.

Fig. 2. Observed (— ● —) and relative (— ○ —) survival after primary mitral valve replacement in patients who survived the first postoperative month; n = 448. 95% confidence intervals at 5 and 10 years and the number (N) of patients at risk are given.
the Swedish Cause of Death Register and a continuously updated population register. By use of these combined registers, all patients could be assigned a date of death or identified as being alive on 31 December 1992.

Total mortality, including death from any cause, was used to calculate relative survival.

2.3. Statistical methods

2.3.1. Early mortality (death from any cause within 30 days postoperatively)

For identification of factors related to the early outcome, logistic regression analysis [15] was used. The odds ratio from this analysis was used as a measure of the relative risk.

2.3.2. Long-term survival (death from any cause after 30 days postoperatively)

The observed survival rate for all causes of death was calculated by the actuarial (life-table) method. To test for equality of the observed survival curves the log rank test was used [17]. The mortality related to valvular heart disease was estimated by computing the relative survival rates, as the ratio of the observed to the expected rate [8,10,11]. The expected survival rates were calculated from life tables compiled from the total population of Sweden stratified by sex, 5-year age group, and 5-year calendar period. The variable denoted the disease-specific annual death risk was computed as the complement of the annual relative survival.

If, for example, mortality in the study group is equal to that expected, the relative survival is 100%. However, if mortality among the operated patients is less than that expected among comparable individuals in the general population the relative survival exceeds 100% and the relative survival curve in a graphical presentation rises.

The multivariate analysis of observed survival was based on the standard Cox continuous proportional hazards model [4] using a stepwise approach. The explanatory variables were used in categorical or categorized form. The relative hazard (RH = \( \exp(\beta_i) \)) was used as a measure of the risk of death in different groups, where \( \beta_i \) is the basic parameter in the Cox model.

3. Results

3.1. Early mortality

One hundred and seventy-two patients (7.3%) died within the first postoperative month. The early mortality was 5.9% after AVR (98/1658), 10.4% after MVR (42/500) and 10.6% after DVR (22/207). The causes of early death are presented in Table 2.

Factors related to early mortality was analyzed by multivariate logistic regression and in a stepwise manner.

In patients undergoing aortic valve replacement, the occurrence of significant coronary artery disease increased the early risk, especially if grafting was not performed (CAD with CABG Odds Ratio (OR) = 1.6, 95% Confidence interval (C.I.) 0.1–2.6, CAD without CABG OR = 2.1, 95% C.I. 1.1–4.9). Advanced NYHA class ((OR) NYHA IV = 2.7, 95% C.I. 1.4–5.3), preoperative atrial fibrillation (OR = 1.9, 1.95% C.I. 1.1–3.4), aortic stenosis (OR = 0.5, 95% C.I. 0.3–0.8), and the use of a mechanical prosthesis (OR = 0.7, 95% C.I. 0.3–0.8) all influenced early mortality.
### Table 3
Factors that influenced late observed survival in the multivariate analysis using the Cox regression model and a stepwise approach

<table>
<thead>
<tr>
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<th>Univariate</th>
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<th>Multivariate</th>
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<td></td>
<td>Relative hazard</td>
<td>95% confidence interval</td>
<td>Relative hazard</td>
<td>95% confidence interval</td>
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<td><strong>Aortic valve group</strong></td>
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<tr>
<td>NYHA*</td>
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<tr>
<td>II</td>
<td>Reference</td>
<td></td>
<td>Reference 2.0</td>
<td>1.2–3.3</td>
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<tr>
<td>IIIA</td>
<td>2.6</td>
<td>1.6–4.2</td>
<td>2.3</td>
<td>1.4–3.8</td>
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<tr>
<td>IIIB</td>
<td>3.4</td>
<td>2.1–5.4</td>
<td>2.9</td>
<td>1.6–5.5</td>
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<tr>
<td>IV</td>
<td>3.9</td>
<td>2.1–7.2</td>
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<td><strong>Lesion</strong></td>
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<td>Insufficiency</td>
<td>Reference</td>
<td></td>
<td>Reference 0.5</td>
<td>0.4–0.7</td>
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<tr>
<td>Stenosis or mixed</td>
<td>0.8</td>
<td>0.6–0.9</td>
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<td><strong>Heart rhythm</strong></td>
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<tr>
<td>Sinus</td>
<td>Reference</td>
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<td>Reference 2.3</td>
<td>1.7–3.0</td>
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<tr>
<td>Atrial fibrillation</td>
<td>2.7</td>
<td>2.1–3.5</td>
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<td><strong>No CABG reference</strong></td>
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<tr>
<td>CAD*, with CABGc</td>
<td>1.5</td>
<td>1.2–1.8</td>
<td>1.3</td>
<td>1.1–1.6</td>
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<td><strong>Age, years</strong></td>
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<tr>
<td>&lt; 50</td>
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<td>1.3–3.5</td>
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<td>60–70</td>
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<td>2.1–5.3</td>
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<td>2.0–5.2</td>
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<td>≥ 70</td>
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<td>2.7–6.8</td>
<td>4.0</td>
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<td><strong>Mitral valve group</strong></td>
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<td>NYHA*</td>
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<td>Reference 1.9</td>
<td>1.4–2.6</td>
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<td>≤ IIIA</td>
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<tr>
<td>≥ IIIB</td>
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<td><strong>Double valve group</strong></td>
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<tr>
<td>Other lesion</td>
<td>Reference</td>
<td></td>
<td>Reference 1.9</td>
<td>1.1–3.3</td>
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<tr>
<td>Pure mitral insufficiency</td>
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*NYHA, New York Heart Association.

bCoronary artery disease.
cCoronary artery bypass grafting.

Independently in the after AVR. Advanced NYHA class (NYHA IIIB OR = 2.8, 95% C.I. 1.4–5.7, NYHA IV OR = 11.4, 95% C.I. 4.5–28.9) increased the operative risk in the MVR group, and female sex (OR = 3.0, 95% C.I. 1.1–8.5) in the DVR group.

### 3.2. Late survival

Among those patients who were alive more than 30 days after operation, the observed survival rates after 5, 10, and 12 years were 85.0, 63.0, and 46.6%.

Observed survival was 63.3% and relative survival 84.0% 10 years after AVR (Fig. 1). Survival was significantly (AVR vs MVR or DVR; \(P = 0.005\) log-rank) lower among those who underwent mitral (Fig. 2) or double valve replacement (Fig. 3). Moreover, survival among MVR patients (10-year observed survival = 55.1% and relative survival = 80.9%) (Fig. 3). This tendency was not statistically significant.

### 3.3. Risk factor analysis

#### 3.3.1. AVR group

Concomitant CABG, advanced NYHA class, preoperative atrial fibrillation, pure aortic regurgitation and higher age increased the late observed survival after AVR independently in the Cox proportional hazards model (Table 3).

The use of relative survival rates tended to modify the difference between the subgroups as compared with observed survival rates (Figs. 4–6). The difference in relative survival rates between patients with aortic regurgitation and those with stenosis was much more pronounced than that in observed survival. After 5 years the difference was 9.6 percentage points for relative and 1.5 percentage points for observed survival and after 10 years these figures were 16.4 and 4.2 percentage points, respectively (Fig. 5).
Concerning age, observed and relative survival showed a similar relationship. However, here the difference in relative survival rates between different subgroups was less pronounced than the difference in observed survival. An exception was the highest age group, i.e. patients aged 70 years or more at surgery. This group showed the poorest observed survival (5 years 78.2%) and the best relative survival (101.9% 95% C.I. 96.1–107.7) (Fig. 7). The relative survival rate indicated better survival among individuals undergoing AVR than expected in the same age group in the general population.

Concomitant CABG increased the risk of mortality. This increase in risk became more apparent over time, especially after approximately 5 years from surgery. Again, the relative survival rates were more informative than the observed survival.

3.3.2. MVR group

NYHA class was the only factor independently related to observed late deaths in the Cox proportional hazards model after MVR (Table 3). Patients in NYHA II appeared to run an additional risk for disease-specific mortality during the first 2 years postoperatively. After that point in time the annual relative survival was close to 100%, i.e. there was no excess mortality (Fig. 8).

3.3.3. DVR group

Mitral insufficiency was the only factor that increased late crude mortality independently in the Cox proportional hazards model after DVR (Table 3). The lower survival rate among patients with mitral insufficiency was confirmed but not enhanced when survival was analysed as relative survival (Fig. 9).
4. Discussion

In this study we used as our control the ‘expected’ survival of the Swedish population. In most instances the survival rates of the patients did not return to the normal expected survival of their age- and sex-matched cohort in the general population. This excess mortality can be explained by a number of deaths from cardiac disease related to the patient’s morbid factors at the time of surgery, e.g. impaired function and morphology of the left ventricle, and from the prosthetic valve-related morbid factors such as anticoagulant-related haemorrhage and thromboembolism. The study results underline the palliative rather than curative potential of heart valve replacement in most patient groups [1,6,18–21].

At least two factors must be considered when the relative survival function [2,5,8] is used to measure the outcome. First, in calculations of the expected survival in the study group it is assumed that the survival in the general population is unaffected by deaths related to the disease under study. Since deaths from heart valve disease are uncommon in the general population, the hazard calculated from relative survival in this study constitutes a fair estimate of the disease-specific hazard. This hazard reflects the excess risk associated with heart valve disease in patients selected to undergo heart valve replacement. Second, patients accepted for heart valve replacement in most patient groups [1,6,18–21].

Fig. 6. Relative survival after primary aortic valve replacement by type of lesion in patients who survived the first postoperative month; stenosis, (—■—) and insufficiency (—□—). 95% confidence intervals at 5 and 10 years and the number (N) of patients at risk after one month, 2, 4, 6, 8 and 10 years are given.

Fig. 7. Relative survival after primary aortic valve replacement by age at operation in patients who survived the first postoperative month; < 50 years (—), 50–60 years (—○—), 60–70 years (— ■ —), ≥ 70 years (— □ —). 95% confidence intervals at 5 and 10 years and the number (N) of patients at risk after one month, 2, 4, 6, 8 and 10 years are given.
surgery are selected with respect to their better overall medical condition concerning non-cardiac diseases at the time of surgery. This is probably more pronounced in the older age-groups and would increase their relative survival rate. Moreover, the present paper is focused on prognosis in patients surviving the immediate postoperative period. Exclusion of deaths within the first month also biases the results in favour of surgery. There is, therefore, a risk that studies of relative survival rates, including the present one, will underestimate the excess mortality rates after heart valve replacement.

Relative survival is computed as the ratio of the observed to the expected among a group of patients with respect to age, sex and time period. There is nothing that prevents the relative survival from being more than 100%. One reason for such a high relative survival is a truly better survival in the studied group, e.g. due to a positively selected patient group. Another reason may be chance effects in small subgroups, particularly towards the end of the follow-up period, when the number of people at risk often is small. Which of the two reasons that is the real one can in general be judged from the pattern of the survival curve and the size of the standard errors (or confidence limits) of the curve.

It is obvious that patient groups defined on the basis, for example, of type of valve replacement, concomitant

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**Fig. 8.** Relative survival after primary mitral valve replacement by preoperative NYHA functional class in patients who survived the first postoperative month. NYHA II (—□—), IIIA (—) ≥ IIIB (—○—). 95% confidence intervals at 5 and 10 years and the number (N) of patients at risk after one month, 2, 4, 6, 8 and 10 years are given.

**Fig. 9.** Relative survival after primary double valve replacement by type of mitral valve lesion in patients who survived the first postoperative month; pure mitral insufficiency (—□—) and any other mitral lesion (—■—). 95% confidence intervals at 5 and 10 years and the number (N) of patients at risk after one month, 2, 4, 6, 8 and 10 years are given.
CABG or not, and volume- or pressure-loaded lesion, differ in many respects [7,12]. Each subgroup may have some specific risk factors and/or specific effect of these. However, patients undergoing open heart surgery, exposed to cardiopulmonary bypass, also have a lot in common, for example, factors related to the bypass technique or management of the myocardial ischemia. Most patients do not have a clear-cut disease or disorder, and the patient materials comprise individuals with different diseases at different stages and combinations of these. The optimal way of performing risk-factor analyses is also a matter of some controversy [16,19]. A separate multivariate analysis in each subgroup is one possible strategy, while analysis of all patients undergoing open heart surgery in one large group, with the aim of identifying interaction effects in certain subgroups is another. Both ways have advantages and drawbacks. The aim of the present study was to provide an overview description of the survival, among all patients after a primary heart valve replacement. We include a multivariate analysis of a number of ‘standard’ demographic risk factors. Further risk factor analysis in concordance with the outlines given above should be performed in order to shed full light on the function of disease-specific mortality.

Our policy has been to bypass all significant stenoses in the coronary arteries. This policy was strengthened when we noted that concomitant coronary artery disease in patients undergoing aortic valve replacement increased the early risk if bypass was not performed [23,24]. This finding was consistent in the present study. We found a tendency towards lower long-term observed survival after concomitant CABG [6,19–21]. However, patients with both diseases, valve and coronary disease, are generally older at the time of surgery. Correction for expected mortality also reduced the difference in survival between patients who underwent concomitant CABG and those who did not.

Atrial fibrillation preoperatively reduced the survival substantially in patients with an aortic lesion [19]. Among patients who underwent aortic valve replacement and had preoperative atrial fibrillation 35% were alive after 10 years, corresponding to an excess mortality of 50%.

This study confirms a trend towards increased excess mortality among patients with volume-loaded valve lesions [1,18]. This was especially apparent with regard to pure aortic regurgitation and concomitant mitral insufficiency. The latter tended to increase the risk in all groups. The results indicate that valve replacement may have been undertaken too late among patients with aortic insufficiency.

Our data emphasize the need to be cautious about earlier surgery for mitral valve replacement. This study showed an excess mortality of 32% among patients who survived the first postoperative month after mitral valve replacement.

We found no evidence to indicate improving results over time in any valve group. However, the fact that the results reflect older surgical techniques must be kept in mind, especially when considering the results in the MVR group [24]. The current surgical methods save the papillary muscle apparatus, completely or partly, and retain more of the normal shape of the left ventricle [22]. This approach probably prevents or delays the onset of chronic congestive failure and consequent premature death after mitral valve surgery [3]. However, the apparent excess risk of premature death after mitral valve replacement, confirmed in our study [1,6,18], supports current efforts to repair the valve whenever possible.

The timing of surgery in patients with heart valve disease is still a matter of some controversy [14,18,19,25]. In the present study patients submitted to aortic or mitral valve replacement with mild or no symptoms had a low early risk and the survival rate was similar for many years to that in the Swedish population at large. Since few patients were in NYHA class II, the estimates may be uncertain and caution must be observed in the interpretation. Most recent studies confirm that marked symptomatic deterioration implies an increased early and long-term risk and excellent survival is achieved for patients in NYHA II [6,19,25]. Some authors therefore advocate earlier surgical intervention [19]. However, even though the operative mortality and morbidity are low in those patients [19,23,24] they are still not negligible considering that a negative outcome affects a more or less asymptomatic individual with at least some years of intact quality of life ahead [25]. Further, early surgery exposes the patient to a number of extra years with a risk of valve-related mortality and morbidity [6,9,13,25].

In fact, patients accepted for surgery on the basis of a significant valve lesion in combination with a recent onset of symptoms (NYHA II) constitute a rather inhomogeneous group [12]. This group varies widely concerning, for example, the degree of advancement or severity of the valve lesion, left ventricular morphology, and systolic and diastolic function. In our opinion, in contrast to those claimed by others, it need not to be concluded that early referral of patients with no or only mild symptoms should be advocated. Symptoms are rather unprecise measures of left ventricular function at exercise. Instead, further investigations must be focused on a search for reliable and reproducible measures useful in the decision regarding the timing for surgery.

References

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Appendix A. Conference discussion

Dr G. Pettersson (Copenhagen, Denmark): You are advocating early operation but at the same time warning against it?

Dr E. Ståhle: It is not that simple that you should recommend earlier surgery. I do not think that symptoms are a good measure. Therefore we should search for other parameters, because symptoms are so imprecise. For example the diastolic LV function at exercise.

Dr R. Karp (Chicago, Illinois): It is a very large series and capable of a number of different analyses. I presume that you did not look at the valve type as to how it influenced survival. The other question is, did you compare in the mitral incompetence group survival those repaired to those replaced?

Dr E. Ståhle: In the aortic valve replacement group, there were four patients who underwent concomitant mitral valve repair. There were no statistical power to analyze the influence of this procedure on outcome. Considering the type of valves, we analyzed the influence of using a bioprosthesis or a mechanical prosthesis. We found no influence in the groups at large. Considering the type of mechanical valve, we used mostly St. Jude valves and Björk-Shiley valves. I do not think there is any reason to assume the use of different types of mechanical valves influence outcome.

Dr C. Yankah (Berlin, Germany): If you look into the natural history of the valve lesions, either mitral or the aortic, the predictors of the long-term survival of patients will depend, e.g. in aortic position on the magnitude of the LV aortic gradients, and the LV muscular mass, hypertrophy or regression of the LV hypertrophy. Did you look into your patients whether they had gradients between the LV, in the left ventricle and aorta, because subsequent regression of the left ventricular wall mass and improvement of LV performance and ejection fraction could then be used also as predictors for long-term survival.

Dr E. Ståhle: Unfortunately I do not have those kind of measures.

Dr C. Yankah: It is very important to know whether in these particular patients the size of the valve you select for implantation is actually going to be beneficial to left ventricular function, which will also predict and also determine long-term survival.

Dr E. Ståhle: That is definitely so. So from now on we are trying to do a Dobutamine echo on every patient who is undergoing an aortic valve replacement, in order to provide us with that kind of information.

Dr S. Large (Cambridge, England): I very much enjoyed your enormous data and found the most fascinating result to be the difference in survival in aorta valve replacement between those in sinus rhythm and those in atrial fibrillation; something that you implied was not a problem in mitral valve replacement. Firstly, did you do any analysis of these two subgroups, and if you did, was the cause of death between those two related to stroke or was it related to heart failure?

Dr E. Ståhle: If I got your question right, you wanted to know if I made a separate analysis for mitral insufficiency and aortic insufficiency?

Dr S. Large: No. The striking point was that you seemed to have an increased risk of death in patients who underwent aortic valve replacement if they were in atrial fibrillation compared to sinus rhythm. You implied that that was not the case for the mitral patients. Maybe I have taken the wrong message.

Dr E. Ståhle: No. There was a small influence of atrial fibrillation but that was not statistically significant in mitral valve replacement. But I looked for interaction effects, and it seems as if atrial fibrillation is especially valid for patients who have aortic insufficiency, but atrial fibrillation also increased the risk for those with a mixed or stenotic lesion.

Dr S. Large: If I could just needle a bit more, my question really is, the mode of death, the increased risk of death in those with aortic valve replacement in atrial fibrillation due to stroke, implying a thromboembolic problem, or is it due to ventricular failure?

Dr E. Ståhle: I have not looked into that.

Dr F. Fontan (Bordeaux, France): My question is complementary to the previous one. Congratulations for the very nice information. But
we are surgeons and we know that the mode of death can influence the preoperative decision in patients on whom we may hesitate to do surgery or not. For example, we know from previous studies that in the early postoperative phase after aortic replacement the patients are in danger of death due to sudden death or ventricular arrhythmias. So I wonder if you have been interested in your study on the mode of death of these patients and if you can give us information on that.

**Dr E. Stähle:** Unfortunately not. We get the information concerning patients being dead or alive from the registry in Sweden, as it is easily available. We can also analyze the cause of death, but the validity of causes of death is not valid 100%. So you have to follow the patients more cautiously, and I think that should also be done as a complement to relative survival analysis. But that kind of information such as morbidity and modes and causes of death, is not possible to obtain from this methodology.