Aortic valve replacement for aortic regurgitation and stenosis, in patients with severe left ventricular dysfunction

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Abstract

Objective: Aortic valve replacement for aortic valve stenosis (AS) and regurgitation (AR) in patients with severe left ventricular (LV) dysfunction contains an increased risk. Few data are available on the outcome of such patients. Methods: Fifty-five consecutive patients with severe LV dysfunction (ejection fraction, EF; <30%) and aortic valve replacement for AS (n = 35) or AR (n = 20) were investigated between 1994 and 2001. EF was 25 ± 5%, mean transvalvular gradient 26 ± 6 mmHg (AS), aortic valve area 0.66 ± 0.18 cm² (AS), cardiac index (CI) 2.4 ± 0.9 l/min/m², enddiastolic LV diameter (LVEDD) 64 ± 8 mm and endsystolic LV diameters (LVESD) was 55 ± 3 mm. Ninety percent of patients were in New York Heart Association (NYHA) functional class III/IV at admission to the hospital. Concomitant coronary artery bypass grafts (CABG) were performed in 14 patients. Follow-up examinations including chest X-ray, echocardiography, exercise testing, were performed among survivors. Results: The survival rates for AS were: 1-year 76%, 2-year 68.8%, 5-year 64.2%; for AR: 1-year 94.4%, 2-year 86.5%, 5-year 74.2%. NYHA functional class improved from 90% in class III/IV to 45 (AR group) and 24% (AS group) at follow-up (P < 0.02). The LVEDD decreased to 54 ± 8 mm after 1 year. The EF improved to 38 ± 4 (AR group) and 40 ± 5% (AS group) at follow-up. Conclusions: Despite severe LV dysfunction, increased 1-year mortality especially in the AS group, aortic valve replacement was associated with improved functional status, symptoms and EF in both groups and in most patients. We, therefore, conclude that aortic valve replacement in patients with severe LV dysfunction can be performed with acceptable risk.

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Keywords: Aortic valve stenosis; Aortic valve regurgitation; Valve replacement; Severe left ventricular dysfunction; Follow-up

1. Introduction

Aortic valve replacement for either aortic regurgitation (AR) or stenosis (AS) carries high risk for adverse events and poor long-term survival, when associated with severe left ventricular (LV) dysfunction, enlarged LV diameters and low transvalvular gradient [1–5]. Despite the reported increased risk of aortic valve replacement in these patients, medical treatment also has more worse survival rates [6,7]. Aortic valve replacement is the only effective treatment, but the operative risk increases in the presence of LV systolic dysfunction [5,8–10].

Few data are available on the clinical outcome of patients with severe AR or AS and poor LV function [8,9,11]. Predictors of postoperative survival and global systolic function after aortic valve replacement have not been clearly identified. Therefore, with this study, we sought to test the hypothesis that aortic valve replacement in patients with either AR or AS and severe LV dysfunction can be performed at an acceptable operative and long-term risk. Less information are available in the literature and the results are conflicting.
2. Methods

From the University Hospital Muenster, 55 consecutive patients, who had aortic valve replacement for either isolated AS or AR in the presence of severe LV systolic dysfunction (ejection fraction, EF; <30%) between 1994 and 2001 were included. Coronary artery disease (CAD) was not an exclusion factor. Preoperative EF was assessed by echocardiography (ECG) and by biplane ventriculography if possible. In the presence of CAD, EF was assessed by radionuclide angiography. Patients were excluded if they had concomitant valvular operations other than aortic valve replacement, a previous aortic valve replacement, or were <18 years old. The medical records of 55 patients who fulfilled the entry criteria for the study including preoperative data, 2D Doppler echocardiographic results, cardiac catheterization hemodynamics and coronary artery anatomy and operative data, were reviewed (Table 1).

2.1. Patient characteristics

Fifty-five patients were included. Of these, 20 patients suffered from AR, and 35 from AS. All patients were included only in the presence of a poor LV function (EF < 30%), low transvalvular gradient (<30 mmHg) and enlarged left ventricle (enddiastolic LV diameter (LVEDD) > 6 cm, endsystolic LV diameters (LVESD) > 5.3 cm). Patient characteristics are described in Table 1. The preoperative symptoms are outlined in Table 2 and operative and postoperative data in Table 3.

Of the 55 patients, six were New York Heart Association (NYHA) class II (10.9%) and 24 NYHA class III (43.6%) and 25 NYHA class IV (45.5%) Fig. 1. Patients in NYHA functional class II were operated on, when aortic valve disease became symptomatic.

2.2. Echocardiography

All patients underwent transthoracic ECG at admission to the hospital by an experienced cardiologist. After

![Table 1](image_url)

<table>
<thead>
<tr>
<th></th>
<th>Aortic regurgitation</th>
<th>Aortic stenosis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>20</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>14/7</td>
<td>21/13</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61 ± 12</td>
<td>67 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>Body surface (m²)</td>
<td>1.92 ± 0.21</td>
<td>1.89 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA-class</td>
<td>3 ± 1</td>
<td>3 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>24 ± 6</td>
<td>25 ± 4</td>
<td></td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.7 ± 1.2</td>
<td>2.1 ± 0.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>2.53 ± 0.38</td>
<td>0.66 ± 0.18</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Transvalvar gradient Δp (mmHg)</td>
<td>23 ± 10</td>
<td>26 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDD (cm)</td>
<td>6.7 ± 0.8</td>
<td>6.2 ± 0.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LVESD (cm)</td>
<td>5.6 ± 0.3</td>
<td>5.4 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.29 ± 0.2</td>
<td>1.32 ± 0.61</td>
<td>NS</td>
</tr>
</tbody>
</table>
Doppler echocardiographic examination. The LV outflow tract area was calculated from the diameter of the outflow tract (area = diameter$^2 \times 0.78$), assuming circulatory geometry. The velocity of the LV outflow tract was obtained by pulsed-wave Doppler ECG from the apical long axis view, and the maximal instantaneous (aortic valve) gradient was calculated from the peak aortic Doppler velocity by the modified Bernoulli equation (pressure gradient = $4 \times$ velocity$^2$). With online software, mean aortic pressure gradient and time velocity integral of the aortic and LV outflow tract flow velocities were measured. Three to five cardiac cycles were measured and the values were averaged. Aortic valve area was calculated with the continuity equation: \( AVA = (LVOT\ area \times LVOT\ TVI)/aortic\ TVI \), where \( AVA \) is aortic valve area, LVOT, LV outflow tract and TVI, time velocity integral. Stress echo with dobutamine in presence of low transvalvular gradients was performed in 14 patients to distinguish severe LV dysfunction and real low transvalvular gradients.

### 2.3. Surgical techniques

All surgical records were reviewed to determine the type and size of aortic valve prosthesis and whether coronary artery bypass grafting (n = 14; 25.4%) or aortic root enlargement (n = 4; 7.2%) was performed concomitantly with aortic valve replacement. Mechanical valves in 49% (St. Jude Medical valves or TEKNA valves; n = 27) and biological valves in 51% (Carpentier Edwards, Peri-mount; n = 28) were implanted. The operative data are outlined in Table 3. Aortic valve replacement was performed in a standardized manner. In all patients, retrograde blood cardioplegia (Buckburg solution) was used.

Thirty patients of the AS group presented intraoperative a real AS, nevertheless in five patients just a moderate AS was found. In 15 patients, a markedly myocardial hypertrophy was observed.

### 2.4. Follow-up

All survivors were retrospectively investigated. The patients were invited to ambulatory controls after telephone interview. Of these, 40 patients were examined during a follow-up time period of 25.8 ± 24.9 months (range 0–89.1 months). Complete follow-up information was available among all survivors. The data record of nine patients who died during follow-up were retrospectively reviewed from the latest ambulatory examination of these patients. The six patients who died within 30 days postoperatively were under clinical control at either our department or peripheral hospitals.

### 2.5. Statistics

Statistical analysis was performed using the statistical software package of social science (SPSS 10.04, Chicago, Illinois, USA). All data were expressed as mean and standard deviation. After logarithmic transformation of the data, a normal distribution could be assumed, and the paired Student’s \( t \)-test was used. The survival curve was analyzed using the non-parametric Kaplan–Meier test and the predictors were analyzed by Cox proportional-hazards model. The relationship between univariate and multivariate potential risk factors with operative mortality (i.e. death within 30 days of operation) was assessed by logistic regression. The relationship of preoperative variables to postoperative EF was assessed by simple and multiple linear regressions. Differences were considered significant at a value of \( P < 0.05 \).

### 3. Results

#### 3.1. Clinical outcome

The 30-day mortality was 10.9% (six of 55 patients)
among patients with aortic valve disease and severe LV dysfunction (EF < 30%) and aortic valve replacement. Of these, all patients suffered from AS with a low transvalvular gradient ($\Delta p < 30$ mmHg). Multifactor failure derived from either cardiogenic shock ($n = 2$) or sepsis ($n = 4$) were found to be the reasons of death in these patients. No 30-day mortality was observed in patients who underwent aortic valve replacement for AR and severe LV dysfunction. The 30-day mortality was, therefore, significantly higher in the AS group ($P < 0.01$). The first death in the AR group occurred after 2.3 months. Fifteen patients died during a mean follow-up of $25.8 \pm 24.9$ months (range 0–89.1 months). Of these, 13 patients died from cardiac reasons (heart failure, arrhythmias) and two from non-cardiac causes (one accident, one cancer).

The survival rate of the AS group was 76.1, 68.8 and 64.2% for 1, 2 and 5 years, respectively (Fig. 3). For the AR group, the survival rate for 1, 2 and 5 years was 94.4, 86.5 and 74.2%, respectively (Fig. 3).

The mean aortic prosthetic size was not different (23 ± 2 vs. 24 ± 3 mm) among survivors compared with non-survivors (NS). No differences regarding the aortic valve type and 30-day mortality were observed. The mean age among survivors was 63 ± 11 years and 69 ± 12 years in non-survivors ($P < 0.05$).

### 3.2. NYHA functional class

Symptomatic improvement was noted in most of the survivors. Ninety percent were severely symptomatic (NYHA class III and IV) before and only 32% after operation ($P < 0.02$; Fig. 1). The significant change in NYHA functional class III/IV preoperatively vs. follow-up was $P < 0.02$.

### 3.3. LV-EF

EF was assessed echocardiographically at follow-up among survivors. All survivors showed a positive change of EF at follow-up. The EF increased significantly in both groups (AR, 24 ± 6 vs. 38 ± 4%, $P < 0.02$; AS, 25 ± 4 vs. 40 ± 5%, $P < 0.02$; Fig. 2).

### 3.4. Left ventricular diameters

LVEDD decreased in the AR group significantly from 6.7 ± 0.7 to 5.1 ± 0.7 cm at follow-up ($P < 0.02$). In the AS group, there was a significant decrease of the LVEDD from 6.2 ± 0.5 to 5.4 ± 0.7 cm at follow-up ($P < 0.05$).

LVESD decreased significantly from 5.5 ± 0.3 cm preoperatively to 4.3 ± 0.4 cm at follow-up ($P < 0.01$), no difference between AR and AS was observed Fig. 3.

### 3.5. Odds ratio (OR)

Independent predictors of mortality, shown by logistic regression analysis of preoperative variables, were creatinine above 1.4 mg/dl (OR, 11.0 [2.34, 56.82]; $P < 0.001$), LVESD > 5.4 cm (OR, 0.24 [0.05, 1.05]; $P < 0.05$), concomitant coronary artery bypass grafts (CABG; OR, 4.12 [0.94, 18.69]; $P < 0.05$) and NYHA class III/IV (OR, 0.14 [0.02, 1.12]; $P < 0.05$).

### 4. Discussion

This retrospective analysis of patients with severe LV dysfunction, who underwent aortic valve replacement for either AS or AR, represents an attempt to establish survival expectations for these patients and to determine the factors that predict poor hospital and long-term survival.

#### 4.1. Aortic stenosis

In severe AS, the left ventricle compensates for chronic pressure overload by hypertrophy in an attempt to normalize wall stress. Initially, EF and cardiac output are maintained. When wall stress exceeds the compensating mechanism, LV systolic function decays secondary to afterload mismatch, and the mean pressure gradient generated by the LV may be low despite the presence of severe AS. Thus, when LV dysfunction is due to afterload mismatch, as seen in severe AS, aortic valve replacement results in improvement in EF symptoms and survival [5,10,12]. LV dysfunction is a major prognostic indicator of the outcome of patients undergoing aortic valve replacement for AS [1,3–5,7,9,10,12,13,15,16]. Aortic valve replacement for AS decreases ventricular afterload, subsequent changes include adaptation and remodeling, with regression of hypertrophy and LV mass [10]. EF, therefore, would be expected to improve after aortic valve replacement in patients with reduced preoperative EF. Those who do not improve probably have fixed

![Fig. 2. Comparison of preoperative and postoperative left ventricular ejection fraction (LV-EF), of aortic regurgitation and aortic stenosis at follow-up. Solid horizontal line indicates mean EF; hatched box, 1SD and vertical line, highest and lowest mean values; *$P < 0.001$.](image-url)
myocardial damage [10]. It has been previously described that patients with preoperative reduced EF, low mean transvalvular gradient and previous myocardial infarction are associated with a lack in improvement of the EF after aortic valve replacement [17]. An improvement in postoperative EF of approximately 15% was noted in our study. These data are in agreement with most authors, the reasons for the absence of improvement in EF have been already described by Connolly and associates [5].

However, the outcome of patients with LV dysfunction who undergo aortic valve replacement is poorly characterized. The survival rate for 68 patients with AS, severe LV dysfunction and low transvalvular gradient have been described by Pereira and coworkers. They found a 1- and 4-year survival rate of 82 and 75%, respectively [7].

This information shows that in a modern era, aortic valve replacement can be performed in this patient population with operative mortality similar to patients with better LV function, reduced albeit clinically acceptable long-term survival [1,7,14]. In our study, the long-term operative results in these patients were certainly gratifying, with an excellent recovery of quality of life, as depicted in Fig. 1, and with 67% of hospital survivors in functional class I or II at follow-up. Our results stand in contrast to previous reports where, we found a similar 30-day mortality, but a slightly greater 1-year mortality, reflecting the remodeling process in the early postoperative period. Patients with potentially irreversible changes in the myocardial structure, probably died due to failure in recovery within 1 year after surgery.

4.2. Aortic regurgitation

Patients with AR develop a compensatory large end-diastolic volume and eccentric cardiac hypertrophy [1]. Chronic AR leads in both, LV pressure and volume overload, imposing a combination of increased preload and afterload on the ventricle [3]. With a severe reduction in diastolic perfusion pressure, a decrease in diastolic coronary flow occurs and some patients may develop angina, especially because myocardial oxygen demand in these dilated hypertrophied ventricles may be very high [1]. The adaptive process leads to myocardial fibrosis, possibly as a result of myocardial ischemia. As aortic insufficiency continues, diastolic wall stress increases without a further increase in wall thickness, and myofibrillar slippage may develop. This process may be ongoing as a spiral event, leading potentially in an irreversible myocardial damage without the possibility of aortic valve replacement. Recent long-term studies demonstrated that improvement of LV function after aortic valve replacement in patients with chronic AR is related significantly to the early reduction in LV dilatation arising from correction of LV overload. In some patients with preoperative severely dilated left ventricles, ventricular dilatation is still present postoperatively. Patients with a LV dysfunction below 30% are of interest in this issue. It has been reported that the majority of

![Kaplan–Meier survival curve for patients with aortic stenosis (n = 35) decreases LV function (EF < 30%), low transvalvular gradient (<30 mmHg) compared with aortic regurgitation (n = 20) and decreases LV function (EF < 30%) and enlarged left ventricle (LVEDD > 60 mm; LVESD > 55 mm).](image_url)
patients with severe LV dysfunction show little improvement in function postoperatively. These patients were declared as the patients with the greatest perioperative risk of death [8,15]. However, the optimal time point for corrections is still under discussion. In this study, we present data of patients with AR and already severely decreased LV function. All patients were asymptomatic for a long time and came to the surgeons after several LV decompensation or symptoms such as syncope and dyspnoea. Duarte and coworkers showed that aortic valve replacement in patients with AR and severe LV dysfunction have been found to be a significant predictor of poor late survival [4]. A 1- and 5-year survival rate of 84–95 and 60–80%, respectively, have been reported [1,3,4,8,16]. We found survival rates of 95 (1 year) and 75% (5 years), which are in line with the literature. We furthermore observed an improvement of the EF and the NYHA class at follow-up. Different findings of the mortality rate may depend on the time point of surgery, the prevalence of symptoms or surgery performed before 1990 [10]. However, as the mid-term survival is above the survival rates following heart transplantation, it is sensible to perform high risk aortic valve replacement in patients with AR and severe LV dysfunction.

### 4.3. Prognostic factors of survival after aortic valve replacement

Several variables have been investigated to identify patients at increased risk of morbidity and mortality after aortic valve replacement. Hospital mortality in these patients has been associated with advanced age, female sex, LV dysfunction, emergency procedure, reoperation, advanced functional classification, renal or hepatic failure, concomitant CAD and non-sinus rhythms [4,7,13,18,19]. Confirming these findings in our study, patients with increased creatinine levels above 1.4 mg/dl and concomitant performance of CABG have had a significant greater risk of mortality.

The relatively high 1-year mortality rate in the stenosis group might depend on either less severe AS (intraoperative findings in five patients) or myocardial hypertrophy associated with an increased risk of arrhythmias and sudden cardiac death. The use of anti-arrhythmic drugs or implantable cardioverter systems should be discussed to improve the survival rates in this group. The rate of emergency valve replacements obviously increases the mortality rate in this group.

### 5. Conclusions

Patients suffered from either AS or AR, associated with severe LV dysfunction present a small but controversial subset. In our retrospective analysis, aortic valve replacement for patients with AS and severe LV dysfunction and low mean transvalvular gradient can be performed with an acceptable operative risk, and despite increased 1-year mortality, good long-term survival rates. Even if our data for AS indicated lower long-term survival rates than after heart transplantation, the high risk aortic valve surgery is due to the donor shortage, a reliable alternative in these patients.

Patients suffering from AR and severe LV dysfunction, increased LV diameters derived benefit from aortic valve replacement with an acceptable mortality rate and a survival rate which is comparable to patients with better LV function.

### References


Appendix A. Conference discussion

Dr A. El-Ghafary (Cairo, Egypt): My question is why you keep them until their ventricular function becomes very deteriorated? Why not to hurry up in performing the surgery earlier than that before the deterioration of LV function?

Dr Rothenburger: The reason is most of these patients are asymptomatic for a very long time, that has been published in a lot of papers, and we saw these patients for the first time in this bad clinical condition. Of course we would have operated on these patients much earlier; of course, you are absolutely right. But I think everybody has these kinds of patients in their clinic.

Dr J. Pirk (Prague, Czech Republic): About preoperative diagnostics, did you perform dobutamine tests on these patients?

Dr Rothenburger: Yes. If it wasn’t sure whether the transvalvular gradient depended on the ventricular dysfunction, we performed a dobutamine echo, as reported in Circulation last year or two years ago.

Dr Pirk: Have you seen any difference in those patients? They increased their gradient?

Dr Rothenburger: No.

Dr M. Radermecker (Liege, Belgium): I applaud your attempt to try to fix a problem which is a difficult one, in my view, but I would like to have your opinion. It is already difficult enough to consider either aortic stenosis that has gone too far and aortic regurgitation that has been taken too late, and I cannot see the rationale for mixing them all, if you want to go ahead with a prognostic factor after surgery, for example. I would just like to have your opinion, please.

Dr Rothenburger: Regarding the prognostic factors we found, we measured the odds ratio and we found creatinine above 1.4 was an important factor and a concomitant coronary artery procedure as well, and we found a much higher mortality rate in these patients, but no difference between the regurgitation or stenosis group after one year.

Dr A. El-Ghafary (Cairo, Egypt): If any of those patients had a coronary lesion, did you perform coronary angiography before you proceed to aortic valve replacement?

Dr Rothenburger: Yes, all patients.

Dr El-Ghafary: None of them had any lesions in the coronary artery?

Dr Rothenburger: In 14 patients we performed an additional CABG procedure.

Dr El-Ghafary: You will repair the deterioration of the left ventricular function to the coronary lesion?

Dr Rothenburger: Yes.

Dr El-Ghafary: or the regurgitation itself or both of them?

Dr Rothenburger: Maybe both lesions.

Dr L. Muller (Innsbruck, Austria): Do you have any results comparing stented and stentless biological valves?

Dr Rothenburger: No. In this group we just used the Perimount valve in the biology group and St. Jude Medical valves in the mechanical group.

Dr A. El-Ghafary (Cairo, Egypt): You just mentioned that there is a lot of improvement of left ventricular function. Did you compare the improvement to the style or the type of the valves that you implanted or not?

Dr Rothenburger: There were just 55 patients, so we didn’t find any difference between the valve types. We were surprised about the improvement of the ejection fraction.