

# Early and long-term outcomes after surgical treatment in patients with aortic stenosis and severe left ventricular heart failure without concomitant coronary artery disease with respect to preoperative mean transvalvular pressure gradient

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## Abstract

**Introduction:** There are limited data on early and long-term prognosis in patients after aortic valve replacement who have left ventricular dysfunction, reduced ejection fraction (EF)  $\leq 35\%$  and no concomitant coronary artery disease.

**Aim:** To assess the prognosis in this group of patients depending on the mean aortic gradient (MAG) value.

**Methods:** This study involved 60 patients with severe aortic stenosis and EF  $\leq 35\%$ . Patients with coronary artery disease, more than moderate aortic regurgitation and any other valvular lesion were excluded. Patients were divided into two groups based on the MAG values: group I included patients with MAG  $\leq 35$  mmHg, and group II included patients with MAG  $> 35$  mmHg.

**Results:** Early mortality after aortic valve replacement was 14.2% in group I, and 5.1% in group II. During a mean follow-up of 48 months mortality in groups I and II was 16.6% and 2.6%, respectively. In the follow-up period, a significant functional improvement according to NYHA scale as well as significant decrease of left ventricular dimensions and increase of EF was observed in both groups of patients.

**Conclusions:** Patients with severe aortic stenosis, left ventricular ejection fraction  $< 35\%$  and MAG  $\leq 35$  mmHg constitute a group of the highest early and long-term mortality risk after valve replacement. In turn, patients with MAG  $> 35$  mmHg should be classified as the group of slightly increased risk.

**Key words:** aortic stenosis, left ventricular failure, postoperative mortality

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## Introduction

In aortic stenosis, blood flow from the left ventricle (LV) to the aorta is obstructed, causing pressure increase in the ventricle. The difference between LV and aorta pressures is called the transaortic pressure gradient. The increase of LV

afterload leads to its compensatory hypertrophy. Increased LV pressure, myocardial hypertrophy and prolongation of outflow time allow normal stroke volume to be provided. However, with the duration of the valve disease and its progression, the systolic function of hypertrophic LV deteriorates and outflow to the aorta

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decreases. This process leads to LV dilatation, heart failure and secondary fall in transaortic gradient. Patients with severe aortic stenosis with severe heart failure constitute a group of very poor prognosis unless surgical intervention is undertaken. However, aortic valve replacement in such patients is associated with high both early and long-term mortality, ranging from 8% to 21%, and, according to different sources, from 21% to 35%, respectively.

The mortality data presented in literature refer to a heterogeneous group of patients, in which 10-51% of patients had previous myocardial infarction (MI) and from 25 to 62% of patients underwent coronary artery bypass grafting concurrently with aortic valve replacement. Analysed patients with severe aortic stenosis had significantly impaired LV ejection fraction (LVEF)  $\leq 35\%$ ; however they differed significantly with respect to the mean aortic gradient (MAG), which is the parameter truly reflecting real LV dysfunction and correlating with postoperative prognosis [1-8].

The aim of the study was to evaluate early and late outcomes after aortic valve replacement in patients with aortic stenosis, LVEF  $\leq 35\%$ , and without concomitant coronary artery disease.

## Methods

The study involved 60 patients with severe aortic stenosis and LVEF  $\leq 35\%$ . All of them underwent aortic valve replacement in the Institute of Cardiology between 1992 and 2004. Patients with significant coronary disease, with previous myocardial infarction, more than moderate aortic regurgitation and with other valvular defects were excluded from the study. In order to compare early and late results patients were divided according to the preoperative MAG value. Patients with MAG  $\leq 35$  mmHg were classified to Group I, and those with MAG  $> 35$  mmHg to Group II. Preoperative characteristics of both groups, based on the data from medical history and echocardiographic examination, are presented in Table I. With respect to the preoperative echocardiographic parameters, LV end-systolic as well as end-diastolic diameter, and also LV end-diastolic volume, were significantly higher in Group I.

Mean follow-up period after the procedure was 48 months (min. 12 and max. 123 months) and comparable in both groups. One subject from Group II was excluded from the analysis due to being lost to follow-up. Early 30-day

**Table I.** Preoperative characteristics of subgroups of patients

Parameters	Group I LVEF $\leq 35\%$ , MAG $\leq 35$ mmHg, n=21	Group II LVEF $\leq 35\%$ , MAG $> 35$ mmHg, n=39
Age [years]	54 $\pm$ 13	59 $\pm$ 11
Women/men [%]	0/100	30/70
Concomitant diseases:		
Arterial hypertension	1 (5%)	4 (10%)
Diabetes mellitus type 2	1 (5%)	3 (7%)
Renal failure	1 (5%)	0
COPD	0	4 (10%)
Previous stroke	0	1 (2%)
Heart failure:		
NYHA class III	13 (65%)	26 (70%)
NYHA class IV	8 (35%)	13 (30%)
Echocardiography		
Left ventricular end-diastolic diameter [cm]	6.9 $\pm$ 0.8	6.5 $\pm$ 0.6*
Left ventricular end-systolic diameter [cm]	6.3 $\pm$ 0.7	5.66 $\pm$ 0.5**
Interventricular septal thickness [cm]	1.2 $\pm$ 0.3	1.3 $\pm$ 0.2
Left ventricular end-diastolic volume [ml]	267 $\pm$ 72	218 $\pm$ 43***
Left ventricular ejection fraction [%]	23 $\pm$ 7	24 $\pm$ 5
Max. aortic gradient [mmHg]	45 $\pm$ 9	77 $\pm$ 19
Mean aortic gradient [mmHg]	27 $\pm$ 5	50 $\pm$ 14
Aortic valve area [cm <sup>2</sup> ]	0.59 $\pm$ 0.1	0.52 $\pm$ 0.1
Duration of follow-up [months]	49 $\pm$ 30	44 $\pm$ 28

Abbreviations: MAG – mean aortic gradient, COPD – chronic obstructive pulmonary disease; in brackets: percent of patients; \* –  $p < 0.01$ , \*\* –  $p < 0.005$ , \*\*\* –  $p < 0.02$

mortality after valve replacement and long-term mortality were analysed. Late deaths were classified according to the cause as cardiovascular (sudden cardiac death, heart failure, cerebral stroke) and non-cardiovascular (cancer). Furthermore, exercise capacity assessed based on the NYHA scale and echocardiographic LV parameters were analysed.

### Statistical analysis

The results are presented as mean  $\pm$  standard deviation or numbers and percentages. Parametric data were analysed using Student's t-test. Statistical significance was set at  $p < 0.05$ .

### Results

Table II depicts early and late postoperative mortality which was significantly higher in group I than in group II. During a long-term follow-up, a significant improvement in exercise capacity according to the NYHA scale, as well as statistically significant decrease of LV diameters and volume, and also an increase of LV ejection fraction, were observed in both study groups (Table III). None of the patients remained in NYHA class IV, and only 3-5% of

patients were in class III. Similarly to the preoperative period, in group I the end-systolic and end-diastolic LV diameter was significantly higher than in group II.

### Discussion

Aortic stenosis contributes to the reduction of coronary perfusion by LV pressure elevation, increasing LV wall tension, and also by the reduction of ascending aorta pressure. Aortic stenosis also leads to an increase of LV mass and, as a consequence, to LV dysfunction, which together with myocardial ischaemia results in severe LV failure. When present, coronary artery disease in such patients escalates LV failure. Early and long-term outcomes depend not only on successful aortic valve replacement, but also on the severity of coronary artery disease, the possibility of concurrent surgical revascularisation and long-term coronary graft patency. To avoid interference of coronary artery disease, hampering interpretation of early and long-term outcomes after aortic valve replacement, patients with previous MI as well as with significant atherosclerotic coronary lesions were excluded from the study.

**Table II.** Early and long-term mortality after aortic valve replacement

Postoperative mortality	Group I LVEF $\leq 35\%$ , MAG $\leq 35$ mmHg, n=21	Group II LVEF $\leq 35\%$ , MAG $> 35$ mmHg, n=39
Early	3 (14.2%)	2 (5.1%)
Long-term cardiovascular	3 (16.6%)	1 (2.6%)
Long-term non-cardiovascular	1 (5.5%)	1 (2.6%)

**Table III.** Functional testing results and echocardiographic left ventricular parameters in long-term follow-up in patients after aortic valve replacement

Parameters	Group I LVEF $\leq 35\%$ , MAG $\leq 35$ mmHg, n=21	Group II LVEF $\leq 35\%$ , MAG $> 35$ mmHg, n=39
Heart failure:	6 (45%)	20 (58%)
NYHA class I		
NYHA class II	7 (50%)	13 (38%)
NYHA class III	1 (5%)	1 (3%)
NYHA class IV	0	0
Echocardiography		
Left ventricular end-diastolic diameter [cm]	5.7 $\pm$ 0.9	5.2 $\pm$ 0.6*
Left ventricular end-systolic diameter [cm]	4.0 $\pm$ 1.1	3.3 $\pm$ 0.7*
Interventricular septal thickness [cm]	1.2 $\pm$ 0.08	1.2 $\pm$ 0.2
Left ventricular end-diastolic volume [ml]	152 $\pm$ 49	128 $\pm$ 12*
Left ventricular end-systolic volume [ml]	73 $\pm$ 48	49 $\pm$ 21*
Left ventricular ejection fraction [%]	52 $\pm$ 14	59 $\pm$ 12*

\* –  $p < 0.05$

Most agree that severe LV failure in patients with aortic stenosis should be diagnosed if LVEF is  $\leq 35\%$  and MAG amounts to 30-40 mmHg [2, 3, 5, 8]. The early mortality observed in such patients varies from 8% to 21% and long-term mortality from 22% to 36% [2, 3, 5, 8]. However, the early mortality of 14.2% in patients with LVEF  $\leq 35\%$  demonstrated in the present study should be compared to the observation of Monin et al., who noted a 14% mortality after aortic valve replacement in patients with lowest incidence of concomitant coronary artery disease [8]. In turn, the long-term mortality of 16.6% observed in our analysis is significantly lower than the mortality of  $>50\%$  found by Monin et al. in a group of the highest risk patients, namely in subjects without preserved contractility reserve in preoperative dobutamine echocardiography [8]. In the remaining studies the incidence of coronary artery disease was as high as 66%, making their reliable interpretation difficult [2, 3, 5].

Preoperative MAG  $>35$  mmHg, even with low LVEF, may indicate preserved LV contractility reserve and can be associated with better prognosis. This has been confirmed by published data reporting early and long-term mortality in this group of patients, ranging from 2.3% to 9.6% and from 5% to 25%, respectively [1, 6, 7, 9]. The findings of Pela et al. on 4.7% postoperative mortality in patients without concomitant coronary artery disease are similar to our result of 5.1% [7]. Early postoperative risk in patients with LV systolic dysfunction and MAG  $>35$  mmHg is slightly higher than early mortality after aortic valve replacement in the general population, estimated to be a mean of 4.1% in Poland, as reported by the Polish Cardiosurgeons Club. Thus, severe aortic stenosis in patients with LVEF  $\leq 35\%$  and MAG  $>35$  mmHg should be defined as pre-decompensatory. In this condition one should expect that myocardial changes including increased myocyte nucleus volume and extent of fibrosis, although of lower importance than previously thought, are less advanced and their normalisation after valve replacement is possible [10].

In both study groups, a significant improvement in exercise capacity classified according to the NYHA scale was observed during long-term follow-up. Furthermore, there was a significant decrease of LV diameters and increase of LVEF assessed by means of echocardiography. These findings are consistent with data of other authors [1-7, 9]. However, significantly greater postoperative LV diameters are observed in patients with low values of preoperative MAG. This may be related to incomplete reversibility of histological changes within the myocardium.

## Conclusions

Patients with severe aortic stenosis, LVEF  $<35\%$  and MAG  $\leq 35$  mmHg constitute a group of the highest mortality in early and long-term follow-up after aortic valve replacement. Patients with MAG  $>35$  mmHg should be classified to the group of slightly increased risk of early mortality in comparison with the general population of patients undergoing aortic valve replacement. Both groups show evidence of significant long-term improvement of heart function, from both functional and echocardiographic assessments.

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# Wczesne i odległe wyniki leczenia operacyjnego u chorych ze zwężeniem zastawki aortalnej i ciężką niewydolnością lewej komory bez współistniejącej choroby wieńcowej w odniesieniu do przedoperacyjnego średniego gradientu przezaortalnego

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## Streszczenie

**Wstęp:** Dysponujemy niewielką ilością danych na temat wczesnego i odległego rokowania u chorych po wymianie zastawki aortalnej z powodu jej stenozy w okresie dysfunkcji lewej komory (LV) z frakcją wyrzutową (LVEF)  $\leq 35\%$  bez współistniejącej choroby wieńcowej.

**Cel:** Ocena rokowania w zależności od średniego gradientu przez zastawkę aortalną (SGA).

**Metodyka:** Do analizy włączono 60 chorych z ciasnym zwężeniem zastawki aortalnej i LVEF  $\leq 35\%$ . Wykluczono uprzednio chorych z chorobą wieńcową, z większą niż umiarkowana niedomykalnością zastawki aortalnej oraz innymi wadami zastawkowymi. Chorzy zostali podzieleni na dwie grupy w zależności od SGA: I – z SGA  $\leq 35$  mmHg, II – z SGA  $> 35$  mmHg.

**Wyniki:** Śmiertelność wczesna po wymianie zastawki aortalnej wyniosła w grupie I – 14,2%, w grupie II – 5,1%. W okresie obserwacji, średnio 48 mies., odnotowano w grupie I 16,6% śmiertelność, zaś w grupie II – 2,6%. W obydwu grupach stwierdzono w okresie obserwacji znamienne poprawę czynnościową w skali NYHA, istotne zmniejszenie wielkości LV, jak również wzrost EF.

**Wnioski:** Chorzy z ciasnym zwężeniem zastawki aortalnej, LVEF  $< 35\%$  i średnim gradientem transaortalnym  $\leq 35$  mmHg stanowią grupę o najwyższym odsetku śmiertelności zarówno wczesnej po wymianie zastawki aortalnej, jak i w obserwacji odległej. Z kolei chorych ze średnim gradientem przez zastawkę aortalną  $> 35$  mmHg należy zaliczyć do grupy nieznacznie zwiększonego ryzyka.

**Słowa kluczowe:** stenoza aortalna, niewydolność lewej komory, śmiertelność pooperacyjna

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