

OUTCOMES OF AORTIC VALVE REPLACEMENT IN AORTIC STENOSIS WITH IMPAIRED LEFT VENTRICULAR FUNCTION: HAS THE TRANSVALVULAR GRADIENT A DETERMINANT VALUE IN THESE RESULTS?

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ABSTRACT

Background: Left ventricular dysfunction remains a major prognostic indicator of the outcome of patients undergoing surgery for aortic valve stenosis (AS). These groups of patients are heterogeneous; they include patients with low and high transvalvular gradient. The aim of this study was to compare the results of aortic valve replacement (AVR) for AS and severe left ventricular (LV) systolic dysfunction in patients with low and high transvalvular gradient and to identify whether the transvalvular gradient has a determinant value in these results.

Methods: In this retrospective bicentric study, 61 patients who underwent isolated AVR for severe AS associated to reduced LV function (LVEF < 40%) were enrolled. The patients were divided into two groups according to the mean transvalvular gradient: group 1 with mean gradient <40 mmHg (n=16) and Group 2 which mean gradient was ≥40 mmHg (n=45). The two groups were similar from demographic characteristics, symptoms, comorbidities and the pathological causes of AS.

Results: The hospital mortality was 12.50% in the group 1 Vs 11% in the group 2 (p=1). Postoperative morbidities were without significant statistical difference between the two groups. In the early postoperative stage, both the groups have improved their LV function.

The post-operative follow-up data in the 2 groups shows no significant statistical difference, in terms of improvement of clinical symptoms and left ventricular features.

Conclusion: The mean transvalvular gradient has a limited prognostic value in the surgical results. Aortic valve replacement may be performed in cases with low transvalvular gradient and is associated with better outcome compared to those with a high gradient.

Keywords: severe aortic stenosis, aortic valve replacement, low transvalvular gradient, left ventricular dysfunction.

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INTRODUCTION

Although left ventricular dysfunction remains a major prognostic indicator of the outcome of patients undergoing surgery for aortic valve stenosis (AS), surgical aortic valve replacement (AVR) still represents the gold standard among the therapeutic options [1].

Dysfunction of the left ventricle (LV) increases the risk of surgery failure significantly but does not constitute a reason to reject these patients [2].

In fact, these groups of patients are heterogeneous; they include patients with low and high transvalvular gradient. The aim of this study was to compare the results of aortic valve replacement for AS and severe left ventricular (LV) systolic dysfunction in patients with low and high transvalvular gradient and to

identify whether the transvalvular gradient has a determinant value in these results.

PATIENTS AND METHODS

Patients:

This retrospective bicentric study, from January 2000 to April 2016, was done at Cardiovascular Surgery Departments of the Avicenna University Hospital and the Military Hospital, both in Rabat (Morocco). It includes 61 patients who underwent isolated AVR for severe AS associated to reduced LV function (LVEF < 40%).

Inclusion criteria were:

- Severe native aortic stenosis with an area < 1 cm² or < 0.6 cm² / m²
- Systolic left ventricular ejection fraction (LVEF) < 40%

Exclusion criteria were:

- Previous aortic valve replacement
- Aortic insufficiency over grade I
- Associated valve disease requiring surgical correction
- Coronary artery disease
- History or clinical evidence of previous acute myocardial infarction
- Less than 18 years old age

The baseline operative risk of the patients was estimated using the logistic EuroSCORE.

Methods:

Patients' data were obtained from the individual patient hospital records.

All patients in our series underwent transthoracic echocardiography (TEE) by an experienced cardiologist

Dobutamine stress echocardiography (DSE) has been performed in 3 cases.

All but one patient underwent coronary angiography—the exceptional patient was operated in extreme emergency after cardiac arrest.

Surgical Management:

Classical aortic valve replacement was performed under general anesthesia and cardiopulmonary bypass (CPB) with moderate systemic temperature, through median sternotomy. Until 2002, myocardial protection was achieved via the administration of intermittent antegrade cold crystalloid cardioplegia (Saint Thomas II) but since 2003, intermittent hyperkalemia cold blood cardioplegia has been employed.

Follow-up:

Early postoperative stage was defined as 6 months after surgery and the late operative stage was defined as the period beyond 1 year after AVR.

Hospital mortality was defined as death at any time before discharge from hospital.

All surviving patients underwent TTE before hospital discharge. During follow-up, patients were contacted directly and were individually requested to make an appointment with the primary surgeon and referring cardiologist. They were investigated by a visit, including physical examination, chest X radiogram, ECG and echocardiogram.

Occasionally, the follow-up data was obtained by telephone contact with their cardiologist.

Statistical analysis:

Standard descriptive statistical methods were used in the analysis. Continuous variables were expressed as means (M) with standard deviation (SD) or medians (MD) with interquartile range (IQR). Student's t-test was used to compare and study the relationships between the continuous variables whenever the data was normally distributed and Non-parametric Mann-Whitney test was used in the others cases. Categorical variables were described as numbers and percentages (%) and analyzed using the χ^2 test or Fisher's exact test, as appropriate. One-way analysis of variance with the post hoc Bonferroni test (for normal distribution with equal variance between the groups) or Friedman test (for non-normally distributed data) was applied to compare quantitative variables between paired samples.

A p-value < 0.05 was considered to be significant.

All the analyses were performed with the Statistical Package for the Social Sciences (SPSS version 11.5, Chicago, Illinois, USA).

RESULTS:

Baseline Clinical Characteristics

Between January 2000 and April 2016, 61 patients, whom 83.60 % were men, underwent isolated AVR for severe AS associated to reduced LV function (LVEF < 40%) in the Cardiovascular Surgery Departments of the Avicenna University Hospital and the Military Hospital, both in Rabat (Morocco). Sixteen patients (26.2%) had a transvalvular gradient < 40 mmHg (Group 1: low gradient) and forty five patients (73.8%) had a transvalvular gradient \geq 40 mmHg (Group 2: high gradient).

The two groups were similar from demographic characteristics including age, gender, body surface area (BSA), presenting symptoms, comorbidities

and the pathological causes of AS. Clinically, there was no significant statistical difference between the 2 groups: the mean NYHA was 2.82 ± 0.80 in group 1 and 3.05 ± 0.72 in group 2 ($p=0.263$). The patients' demographic characteristics appear in Table I. The preoperative echocardiographic patients' data were with significant statistical difference concerning the mean transvalvular gradient and the mean left ventricular end systolic diameter (LVESD).

The mean transvalvular gradient was 30.37 ± 5.80 mmHg in the group1 and 55.80 ± 16.60 mmHg in the group 2 who had a low mean LVESD than the low gradient group.

There was no significant statistical difference concerning the mean calculated logistic EuroScore in the two groups. The preoperative echocardiographic patients' data appear in Table I.

Table I: Comparison of preoperative data between low and high transvalvular gradient groups.

Variables	Group 1		p Value (n=61)
	Low gradient (n=16)	High gradient (n=45)	
Age ¹ (years)	57.20 ± 10.4	58.60 ± 13.20	0.70
Sex ³ Male/Female	14/2 (87.50 %)	37/8 (82.20)	1
BSA ¹	1.80 ± 0.14	1.74 ± 0.16	0.16
NYHA ¹	2.82 ± 0.80	3.05 ± 0.72	0.263
- NYHA ³ II	5 (31.30%)	13 (2.90 %)	
- NYHA ³ III	6 (37.50 %)	21 (46.70 %)	
- NYHA ³ IV	5 (31.10 %)	11 (24.40 %)	
Angina pectoris ³	4 (25 %)	16 (35.60 %)	0.44
Syncope ³	1 (6.30 %)	4 (9 %)	1
Congestive heart failure ³	4 (25 %)	6 (13.30%)	0.43
Etiologies ³			0.14
-Degenerative	7 (43.80 %)	32 (71 %)	
-Rhuematic	8 (50 %)	12 (27 %)	
-Congenital	1 (6.30 %)	1 (2 %)	
Comorbidites ³			
-Hypertension	3 (18.80 %)	15 (33.30 %)	0.35
-Diabetes	3 (18.80 %)	5 (11 %)	0.42
-Renal failure	4 (25 %)	7 (15.60 %)	0.45
-AIS	0 (0%)	1 (2.20%)	1
CT index ²	$0.6 [0.58 ; 0.60]$	$0.60 [3 ; 40]$	0.42
Aortic valve area ¹	0.60 ± 0.20	0.63 ± 0.17	0.60
Mean transvalvular gradient	30.37 ± 5.80	55.80 ± 16.60	<0.001
Preoperative LVEF ¹ (%)	29.60 ± 9.60	34 ± 6.60	0.09
Preoperative LVEDD (mm) ¹	66.80 ± 10	62.50 ± 8.70	0.10
Preoperative LVESD (mm) ¹	55 ± 10	48.50 ± 7.7	0.009*
SPAP ¹ (mmHg)	$46.30 \pm 27,70$	48 ± 20	0.78
Logistic regression Euroscore ¹	11.60 ± 4	8.20 ± 2.60	0.37

1: expressed as means standard deviation (SD); 2: expressed as medians with interquartile range (IQR); 3: described as numbers and percentages (%). BSA: body surface area; AIS: Acute ischemic stroke; CT: cardio-thoracic; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; LVEF: left ventricular ejection fraction; SPAP: systolic pulmonary arterial pressure.

Operative and early postoperative results

The mean prosthesis size was 21.70 ± 1.60 mm in the group 1 and 22.60 ± 1.70 mm in the group 2. The mean aortic cross-clamp time was 61.70 ± 15 minutes in the group 1 and 69.30 ± 22.30 min in the group 2 ($p=0.20$), whereas the average duration of cardiopulmonary bypass (CPB) was 98.30 ± 49.40 min in the group 1 and 104.60 ± 39.80 min in the group 2 ($p=0.60$).

There was no significant statistical difference concerning the early postoperative outcomes. The hospital mortality was 12.50% (2/16) in the group 1 Vs 11% (5/45) in the group 2 ($p=1$)

In the two groups, the causes of deaths were low output syndrome. The mean length of stay in the intensive care unit was 90.40 ± 31.80 hours in the group 1 and 66.4 ± 30.40 hours in the group 2 ($p=0.29$). Postoperative morbidities were without significant statistical difference between the two groups. The inotropic drug support was needed in 93.80% of Group 1 versus 91% of group 2. The use of hemodynamic support by intra-aortic balloon pump (IABP) was necessary in 2 patients (2.50%) of the group 1.

In the early postoperative stage, both the groups have improved their LV function.

Perioperative data are shown in Table II.

Tableau II: Comparison of perioperative data between low and high transvalvular gradient.

Variables	Group 1	Group 2	p Value (n=61)
	Low gradient (n=16)	High gradient (n=45)	
X clamp time¹	61.70 ± 15	69.30 ± 22.30	0.20
CPB time (mn) ¹	98.30 ± 49.40	104.60 ± 39.80	0.60
Biological prosthesis	3(18.70%)	8 (17.80 %)	1
Mechanical prosthesis	13(81.25 %)	37(82.22 %)	1
Prosthesis size (mm) ¹	22.60 ± 1.70	21.70 ± 1.60	0.06
Use of positive inotropic agents³	15 (93.80 %)	41 (91 %)	1
IABP³	2 (2.50 %)	-	0.06
Mechanical ventilation time² (h)	8.50 [5.70 ; 19.20]	10 [8 ; 17]	0.29
IUC stay¹ (h)	90.40 ± 31.80	66.4 ± 30.40	0.29
Early postoperative LVEDD¹ (mm)	64 ± 11.40	60.50 ± 7.70	0.29
Early postoperative LVESD¹ (mm)	49 ± 11.30	46 ± 7.60	0.33
Early postoperative LVEF¹	38.20 ± 11.30	38.20 ± 8.60	0.98
Mean transprosthesis gradient¹ (mmHg)	12.40 ± 4	12 ± 3.40	0.76
Complications			
-Bleeding ¹ (ml)	364.70 ± 216.40	452.45 ± 269	
-Low output syndrome ³	9(56.20 %)	16 (35.50 %)	0.26
-Acute renal failure ³	1 (6.30 %)	1 (2.30 %)	0.44
-Third degree AV block ³	-	2 (4.70 %)	0.40
-Reoperation for bleeding ³	-	1 (2.30 %)	
Mortality³	2 (12.50 %)	5 (11%)	1

1: Expressed as means standard deviation (SD); 2: Expressed as medians with interquartile range (IQR); 3: Described as numbers and percentages (%). X clamp: cross clamping; CPB: cardiopulmonary bypass; IABP: intra-aortic balloon pump; ICU: intensive care unit; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; LVEF: left ventricular ejection fraction; AV: atrioventricular.

Long-term outcomes

After a median follow-up of 40 months (IQR [29; 79.50]) in the group 1 and 36 months (IQR 36 [17; 115]) in the group 2, incidence of late death and complications were similar in the 2 groups. We have recorded 3 deaths, one in the group 1 and two in the group 2 (due to hemorrhagic stroke in one case of the group 1 and due to cancer in the two cases of the group 2).

Among the 52 survivors, 38 patients were audited. The post-operative follow-up data in the 2 groups shows no significant statistical difference, in terms

of improvement of clinical symptoms and left ventricular features.

The NYHA class improved from 2.82 ± 0.80 to 1.10 ± 0.30 in the group 1 and from 3.05 ± 0.72 to 1.20 ± 0.40 in group 2.

Recovery of LV systolic function was also apparent in the 2 groups. The group 1 had recovered 25.40 ± 0.40 points of EF. In Group 2, the gain was 15.40 ± 2 points.

Decrease of LV diameters was also apparent in the 2 groups. Table III shows the long-term outcomes of the two groups.

Table III: Comparison of long-term outcomes between low and high transvalvular gradient.

Variables	Group 1	Group 2	p Value (n=61)
	Low gradient (n=16)	High gradient (n=45)	
Controlled patients³	8 (57%)	31 (77.50 %)	0.17
Follow up time ² (months)	40 [29 ; 79.50]	36 [17 ; 115]	
NYHA¹	1.10 ± 0.30	1.20 ± 0.40	0.81
Use of digitalo-diuretic tretement³	1 (14.30 %)	11 (36.70 %)	0.38
Late complications³			
- Cerebrovascular accident	-	2 (6.50 %)	0.29
- Congestive heart failure	-	2 (6.50 %)	
Late postoperative LVEDD (mm)¹	52 ± 12.11	54.60± 7	0.626
Late postoperative LVESD (mm)¹	38.85 ± 11.70	39.43 ± 6.50	0.904
Late postoperative LVEF¹ (%)	55 ± 10	49.20 ± 9.30	0.154
Late death³	1 (12.50 %)	2 (6.50 %)	0.50

1: expressed as means standard deviation (SD); 2: expressed as medians with interquartile range (IQR); 3: described as numbers and percentages (%). LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; LVEF: left ventricular ejection fraction.

DISCUSSION

This study showed that the results of AVR in patients with severe AS, severe LV dysfunction, and low transvalvular gradient were beneficial and comparable to those of patients with a higher transvalvular gradient.

Patients with LV dysfunction represent up to 26% of patients with AS and their spontaneous prognosis is severe [3,4]. Currently, the only effective therapy is the removal of the mechanical obstruction by aortic valve replacement (AVR) or by percutaneous aortic valve replacement (PAVR) as a therapeutic option [5].

Despite the operative risk remains significantly higher, the postoperative prognosis of these patients remains better, compared to those treated medically [6,7]. In our study, the rate of hospital mortality reached the margin of 8-21% reported in the literature [6,8]. (12.50% in the group of low gradient and 11% in the group of high gradient). It was mainly due to low cardiac output.

Literature reports several factors which are considered as associated with unacceptable risk of operative mortality. They include: age, female gender, class III-IV of NYHA, renal failure, congestive heart failure, LVESD > 54mm, severe pulmonary hypertension, absence of contractile reserve (CR) and low trans-aortic valvular gradient [1,8-12]. However most of those series are heterogeneous, including patients with other associated lesions, especially, coronary or valvular disease other than aortic stenosis.

In fact, prior acute myocardial infarction, concomitant coronary artery bypass graft surgery and untreated coronary lesions are considered as significant risk factors of hospital mortality as far as mitral valve regurgitation (MR) [1, 7, 13].

To avoid biases of the association with others disease lesions, our study has been focused on isolated AS with severe left ventricular dysfunction.

Clavel et al reported that patients with low transaortic gradient were a high-risk population with an operative mortality rate of 18%. The risk was even higher when transvalvular gradient was ≤ 20 mmHg [14].

Our study did not show any significant differences in hospital mortality between patients with low and those with high transaortic gradient. This finding is consistent with those of Borowski et al. they showed a comparable postoperative mortality rate in a low gradient group and a high gradient one [15].

LV contractile reserve (CR), assessed by dobutamine stress echocardiography, can be useful to assess anatomic severity and prognosis. Indeed, the lack of CR increase the hospital mortality and yet should not be considered by itself as surgical contraindication since the potential of myocardial recovery after surgery are not excluded [16-18].

Since 2012, we have begun to study the CR of LV by echocardiography with low-dose of dobutamine. Only three of our patients underwent this test. All of them had a contractile reserve.

In our series, late mortality rate was similar in the two groups. All deaths were related to non-cardiac origin.

Several risk factors of late death have been reported, they include: male gender, advanced age, diabetes mellitus, severe pulmonary hypertension, preoperative class III and IV NYHA, preoperative use of high doses of diuretic, preoperative circulatory assistance by intra-aortic balloon pump and prosthesis-patient mismatch [19-22].

In our study, LVEF, LVEDD and LVESD evolved favorably during early and late postoperative periods in both groups. Recovery of the ventricular function displayed no statistically significant between the two

groups and improvement of clinical symptoms was real in both groups. Some studies have retained our finding; Thus, Vaquette et al confirmed that early postoperative recovery of LV function was associated with significantly greater relief of symptoms and longer survival. They concluded that patients who improve their LVEF more than 10 units in the early postoperative course had a better long-term survival than patients who did not [23- 25]. In our study, LVEF increased in the early postoperative stage but did not reach the threshold of 10 units (8.6 ± 1.7 units in group 1 and 4.2 ± 2 units in group 2) and seemed to be associated with improved survival rate.

CONCLUSION

Despite severe left ventricular dysfunction, aortic valve replacement in aortic stenosis can be tenable with excellent results.

The mean transvalvular gradient has a limited prognostic value in the surgical results. Aortic valve replacement may be performed in cases with low transvalvular gradient and is associated with better outcome compared to those with a high gradient.

The long term outcome of AVR for severe and isolated AS with left ventricular dysfunction and low transvalvular gradient is excellent as evidenced by: Better survival (although the rate of hospital mortality is still for further improving), decreased left ventricular diameters and improvement in left ventricular function and functional class.

Conflicts of interest

The authors declare having no conflicts of interest related to this article

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