The effects of severe aortic stenosis and high pulmonary artery pressure on aortic valve replacement

Faruk Toktas¹, Arif Gucu¹, Gunduz Yumun¹, Cuneyt Eris¹, Serhat Yalcinkaya², Mehmet Demir³#, Tuğrul Goncu¹, Senol Yavuz¹

¹Cardiovascular Surgery Department, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey
²Thoracic Surgery Department, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey
³Cardiology Department, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey
Email: #drmehmetd@gmail.com

Received 2 July 2013; revised 12 August 2013; accepted 1 September 2013

Copyright © 2013 Faruk Toktas et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Pulmonary hypertension development in pure severe aortic stenosis is a situation that affects mortality and morbidity. Material and Methods: Data from files of 31 patients with systolic pulmonary artery pressure over 50 mm Hg and with pure severe aortic stenosis, and underwent aortic valve replacement in our clinic were examined retrospectively. Results: Preoperative effort capacities of the patients were evaluated as follows according to NYHA; 4 patients class 1-2, 16 patients class 3, and 11 patients class 4. Twenty-five metal, and 6 biologic aortic valves were used. Postoperative hospital mortality was recorded as 12% with 4 patients. Patients were re-evaluated on the postoperative 2nd and 12th months. Pulmonary arterial pressure of the patients was measured using echocardiography. Preoperative average pulmonary artery systolic pressure was measured as 55 ± 3 mmHg. The average pressure was measured as 41 ± 3 mmHg on the 2nd, and as 37.8 ± 4 mmHg on the 12th month. The effort capacity evaluation in the postoperative 2nd month was as follows: 11 patients class 1-2, 12 patients class 3, and 4 patients class 4. The effort capacity evaluation conducted in the 12th month was: 14 patients were class 1-2, 10 patients were class 3, and 2 patients were class 4. During the follow-up 1 year, survival rate of the patients was determined as 83.8% average, 5 year survival rate was determined as 61.5%. Conclusion: We believe that AVR may be performed in severe aortic stenosis cases with high pulmonary pressure with acceptable mortality, leading to a better quality and longer life.

Keywords: Aortic Valve Stenosis; Pulmonary Hypertension; Heart Valve Prosthesis Implantation; Prognosis

1. INTRODUCTION

Cases with aortic valve area below 0.6 cm²/m² are accepted as severe aortic stenosis (AS) [1,2]. In several publications, it is stated that the natural course of severe AS is significantly bad [3-5]. Presence of pulmonary hypertension (PH) in severe aortic stenosis is a prognosis negative indicator [6]. The negative prognosis indicators limiting surgery include: narrow aortic valves, left ventricle function disorder, severe aortic stenosis with low aortic valve gradient, severe aortic stenosis with pulmonary hypertension development, and aortic stenosis with cardiac arrhythmia [6-8]. Among these risk factors, lesser and incomprehensive series were published in the literature in regards to implementation of aortic valve replacement (AVR) in pure severe aortic stenosis with pulmonary hypertension when compared to the other factors.

In our study, we aimed to assess the effect of pulmonary hypertension development in severe aortic stenosis on aortic valve surgery results.

2. PATIENTS AND METHODS

Data from the files of the cases underwent aortic valve replacement with systolic pulmonary pressure over 50 mmHg and with pure severe aortic stenosis, in our clinic between the years of 1996 and 2011 were examined retrospectively.

The inclusion criteria were:

1) Severe aortic stenosis and pulmonary artery systolic pressure over 50 mmHg due to aortic stenosis.

*Conflict of interest: none declared.
#Corresponding author.
2) Tricuspid regurgitation flow rate higher than 3.8 m/sn.
3) No evidence of additional valve disease except for tricuspid insufficiency developing secondary to pulmonary hypertension. [While selecting, cases with mitral narrowness (valve area larger than 2.5 cm²), more than first degree mitral insufficiency) or, more than first degree aortic regurgitation were not included in the study group].
4) No accompanying congenital anomalies.

Patients with former valve surgery, and/or previous cardio-vascular surgery, were excluded. Those with accompanying coronary lesions were included in the study. During the same session proper grafts were placed in the required veins and by-pass was conducted. Patients with developed tricuspid insufficiency were included in the study. During the same session De Vega annuloplasty and proper tricuspid annuloplasty were applied to necessary patients.

3. OPERATIVE TECHNIQUE

General anesthesia was administered to the patients through standard balance anesthesia technique. Propofol, and dormicum were preferred for the induction of the patients. Norcuron and/or pancuronium were used as muscular relaxant. Inhalation anesthetics were used when required and isofluran, and/or sevorenin were preferred. Fentanyl citrate was used as narcotic analgesic. Upon anesthesia induction right cardiac catheterization was implemented in all patients with swan-ganz catheter (model 131H-7F; Baxter Healthcare Corp., Edwards Div., Irvine, Calif.). Pulmonary artery pressure was monitored. Heparin was given at 3 mg/kg dose, and heparinization was performed as ACT (activated clotting time) over 480 seconds. During our operations (Pemco Inc., Cleveland, OH, USA) Roller pump, (membranous oxygenator) hollow-fiber membrane oxygenator (Edwards VitaleTM, Edwards Lifesciences LLC, One Edwards Way, Irvine, CA, USA) were used. Medium level hypothermia was used in the patients (average 30°C - 32°C). In cardiac arrest (Plegisol, Abbott Laboratories, North Chicago, IL) crystalloid cardioplegia was used. For maintenance cardiac arrest was continued through cold blood cardioplegia with intermittent potassium and sodium bicarbonate addition in antegrade way with 20 minute intervals.

After standard cannulation process, cardiopulmonary bypass was initiated and aortic valve replacement was performed by single stitches by using suture technique with pledgets 2/0 braided polyester non absorbable stitch.

3.1. Statistical Analysis

Statistical evaluation was conducted by using SPSS 9.0 programs. Student’s t test and $X^2$ tests were used in analyzing variances. Kaplan-Meier analysis was used for survival expectation analysis. A p value <0.05 was accepted as significant.

3.2. Findings

There were 31 patients meeting the inclusion criteria. Twelve of these patients were female (38.7%), and the remaining 19 were male (62.3%). Mean ages of the patients was 53.0 ± 2.3 years (range 38 - 79). Demographic characteristics of the patients are given in Table 1.

Preoperative effort capacities of the patients were evaluated as follows according to NYHA: 4 patients class 1-2, 16 patients class 3, and 11 patients class 4.

During operation, 25 metal aortic valves varying between 19 - 25 in size from various manufacturers (e.g. Carbomedix, St-Jude Medical, and Medtronic), and 6 biologic aortic valves were used. In 5 patients, Manougian procedure for aortic root enlargement was performed due to narrow aortic root. In 12 patients with coronary artery disease, coronary artery bypass grafts were added to procedure during the same session. De Vega Tricuspid annuloplasty was performed using 2/0 prolene in 12 patients with tricuspid insufficiency at 3 - 4 level.

We did not have any perioperative mortality. In one patient with additional coronary bypass grafting, we needed intra-aortic balloon pump for pump retrieval.

Average intubation period was 4.5 ± 1 hours. In two cases we had a prolonged intubation period exceeding 48 hours.

Table 1. Demographic characteristics of the patients.

<table>
<thead>
<tr>
<th>Demographic characteristics of the patients</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (average)</td>
<td>38 - 79 (53.0 + 2.3)</td>
</tr>
<tr>
<td>Gender male/female</td>
<td>12/19</td>
</tr>
<tr>
<td>Hypertension</td>
<td>60%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>17%</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>38%</td>
</tr>
<tr>
<td>Chest pain (angina)</td>
<td>55%</td>
</tr>
<tr>
<td>Renal failure (creatin &gt; 1.8)</td>
<td>27%</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>55%</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (COAH)</td>
<td>12%</td>
</tr>
<tr>
<td>Aspirin use</td>
<td>52%</td>
</tr>
<tr>
<td>Beta blocker use</td>
<td>22%</td>
</tr>
<tr>
<td>Angiotensin converting enzyme inhibitor use</td>
<td>38%</td>
</tr>
<tr>
<td>Statin use</td>
<td>27%</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressure (mmHg)</td>
<td>55 ± 3</td>
</tr>
</tbody>
</table>
Pulmonary arterial systolic pressure measurements of all patients were conducted by swan-ganz catheter placed upon general anesthesia administration. Measurement was repeated on the postoperative 24th hour. Pulmonary arterial systolic pressure measurements and changes are given in Table 2. Preoperative average pulmonary arterial systolic pressure measurements value was measured as 55 ± 3 mmHg. There was a difference between the measurement at preoperative catheter laboratory and preoperative operation table. Surgery room measurements were taken under general anesthesia, following a 6-hour period of starving, therefore these measurements were lower. Thus, we used the values measured during angiography in the study. The postoperative 24 hours average pulmonary arterial systolic pressure measurements value of the patients was determined as 43 ± 5 mmHg. Variance was calculated as 25.38% (p < 0.001).

Hospital mortality was experienced in 4 patients (12%). In two cases the cause of death were the prolonged intubation due to respiratory failure, and accompanying multiple organ failure. One case died during laparatomy secondary to mesenteric ischemia, and severe intestinal resection. One case died due to low cardiac flow.

During the 12-month follow-up, another case died due to extra cardiac reasons.

Patients were reevaluated in the postoperative 2nd and 12th months. Pulmonary arterial systolic pressure of the patients were measured using echocardiography (Vivid 7, GE Medical Systems, Vingmed, Horton, Norway). The average pulmonary artery systolic pressure were measured as 41 ± 3 mmHg on the 2nd month, and as 37.8 ± 4 mmHg on the 12th month, respectively.

The average follow-up was 5.2 patient years, and 88.4% of the patients were followed between 6 months and 13 years. During the follow up period, the 1-year survival rate was determined as 83.8%, and 5-year survival rate was determined as 61.5%.

Ejection fractions of the patients were measured on preoperative, early postoperative (within 2 weeks following surgery), postoperative 2nd month, and 12th month periods. While the preoperative ejection fraction average was 38% ± 18%, this value was obtained as 42% ± 23% during early postoperative period, as 43% ± 20% at the 2nd month, and as 46.6% ± 3% at the 12th month (Table 2).

Patients were evaluated according to NYHA criteria in terms of effort capacities during the same period. Results obtained in the effort capacity evaluation during postoperative 2nd month were as follows: 11 patients class 1-2, 12 patients class 3, and 4 patients class 4. During the effort capacity evaluation at the 12th month 14 patients were class 1-2, 10 patients were class 3, and 2 patients were class 4.

4. DISCUSSION

Cases below 0.6 cm²/m² with valve area in aortic narrowing are accepted as severe aortic stenosis [1,2]. Various publications are available reporting on high mortality rates for severe aortic stenosis cases when valve replacement is not conducted [9-11]. Congestive heart failure emerges significantly in severe aortic stenosis cases within average two years [4]. In AS cases, left ventricle hypertrophy is the reason for severe cardiac arrhythmia and sudden death [12]. Low left ventricle ejection fraction in complex and frequent ventricle arrhythmias and increased peak systolic wall stress are common in Cardiac arrhythmias [13,14]. An important determinant of sudden death in aortic stenosis is the pulmonary hypertension developed parallel to left ventricle function disorder [15]. Positive effect of AVR on patient survival and ejection fraction in severe aortic stenosis are revealed in several studies [16,17].

Table 2. Preoperative postoperative measurements and variances of the patients.

<table>
<thead>
<tr>
<th>Measured values</th>
<th>Preoperative average values n = 31</th>
<th>Postoperative early period average value</th>
<th>Postoperative second month average value n = 27</th>
<th>Postoperative twelfth month average value n = 26</th>
<th>Preoperative measurement-postoperative 12th month measurement variance rate</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery systolic pressure (mmHg)</td>
<td>58.3 ± 7</td>
<td>43.5 ± 5</td>
<td>41.3 ± 3</td>
<td>37.8 ± 4</td>
<td>35.16%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Injection fraction %</td>
<td>34 ± 4.8</td>
<td>42 ± 2.3</td>
<td>43 ± 2.1</td>
<td>46 ± 3.4</td>
<td>34.59%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.68</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic gradient (mmHg)</td>
<td>68 ± 16</td>
<td></td>
<td>22</td>
<td>21</td>
<td>69.19%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Septum thickness (cm)</td>
<td>1.5 ± 0.2 cm</td>
<td>1.46 ± 0.3 cm</td>
<td>1.38 ± 0.2 cm</td>
<td>8%</td>
<td></td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Posterior wall thickness (cm)</td>
<td>1.2 ± 0.1 cm</td>
<td>1.18 ± 0.2 cm</td>
<td>1.16 ± 0.2 cm</td>
<td>0.4%</td>
<td></td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Left ventricle end-diastolic diameter (cm)</td>
<td>5.2 ± 0.8</td>
<td></td>
<td>4.7 ± 0.8</td>
<td>9.6%</td>
<td></td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Tricuspid regurgitation flow rate</td>
<td>3.97 ± 0.5</td>
<td></td>
<td>2.7 ± 0.8</td>
<td>29.97%</td>
<td></td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>
significant recovery observed in our study results in terms of patient ejection fractions. While the preoperative ejection fraction average was 38% ± 18%, this value was obtained as 42% ± 23% during early postoperative period, as 43% ± 20% at the 2nd month, and as 46.6% ± 3% at the 12th month.

Johnson et al. [18] published the first AVR experience in severe aortic stenosis cases with severe pulmonary hypertension in 1988. Later Tracy [19] and Snopek [20] published the series which were not comprehensive and with low mortality results. More extensive case series and randomized studies were conducted by Malouf et al. In his study, AVR was performed on 37 patients with severe aortic stenosis cases developed severe pulmonary hypertension were compared to AVR not-implemented on 10 patients. During the study, operative mortality was reported as 6 (16%), and late mortality was reported as 9%; total 32% mortalities were reported. Eight of the patients treated by conservative treatment died (80%). In our study mortality was 12% and is in accordance with the mortality rate of severe aortic stenosis with left ventricle function disorder reported in the literature [8,17,21].

In the comprehensive study conducted by Ramdas et al. [22], AVR with conducted group and AVR without conducted group of patients with average age 75, average pulmonary artery pressure 69 mmHg with severe aortic stenosis were compared. In AVR not conducted group, 1-month mortality was reported 30% and 1-year mortality was determined as 70%. Renal failure, old age, heart failure, dementia, low ejection fraction were noted as the important causes of mortality. In the same study 1-month mortality rate of AVR conducted group of patients was 8%, 5-year mortality rate was determined as 65%. For AVR not conducted patients, 5-year survival rate was 20%. These significantly successful results display the beneficial results of AVR. However, we believe that the case of Ramdas et al. [22] including the mitral valve attempts in addition to aortic stenosis is an important detail. Implemented mitral valve attempts might affect the reveal of the AVR effect on pulmonary hypertension regression.

During the follow-up of medium and severe aortic stenosis cases with no AVR implementation conducted by Chizner et al. [3], mortality speed was determined as follows: 26% for the 1st year, 48% for the 2nd year, and 57% for the 3rd year. In various studies, 5-year mortality rate differs between 18% - 50% follow-ups of 453 patients with severe aortic stenosis with no AVR implementation conducted by Padmini et al. The survival rates of 1 year, 5 years and 10 years were found respectively as 62%, 32%, and 18%. In our study, 1-year survival rate was 83.8% and 5-year survival rate was calculated as 61.5%.

Long follow-up period and long follow-up results of studies conducted by Ramdas et al. [22] and Malouf et al. [21] are close to our study, however, the average age is higher than our study group. The most important reason why patient average age in our study is younger than that of other studies is that we face cardiac valve diseases earlier than Western societies due to common rheumatic heart diseases in our population. This situation seems to be the reason why the average age of the patient population included in our study is much younger than the series in the literature. (While the etiology of the aortic valve disease in our patient group is mostly formed by rheumatic heart disease, senile degeneration is observed as the most etiologic factor in the series included in the literature.) Moreover, survival length of our patients can be explained by employing relatively younger patient population.

Today cardiac surgery increases in number and finds a place for itself in more common and expanded indications by pushing the limits restricting indications. In most publications, positive results of eliminating the mechanical problem in aortic valve are declared almost in all situations of aortic valve surgery. Most cases scaring the surgeons are published with tolerable mortality and morbidities. We believe that AVR with acceptable mortality can be conducted in severe aortic stenosis cases with high pulmonary pressure and accordingly patients might have much more qualified and longer lives.

**Limitations of the Study**

The most important limitation of our study was that the difference between pulmonary artery pressure levels and primary pulmonary hypertension could not be determined clearly. This might have been determined by taking biopsy from the patients in pulmonary vascular bed, however, we did not have the chance to execute biopsy. The small samples sum is another limitation.

The difference between the effect of revascularization on myocardial performance and clinical regression in the cases with coronary artery diseases included in the study could not be revealed.

Comparison of our study was conducted in surgical cases. Comparison with the patients receiving medical treatment was realized with the help of the results of medical treatment cases given in the literature.

**REFERENCES**

http://dx.doi.org/10.1016/0735-1097(89)90047-8

http://dx.doi.org/10.1016/0002-8703(80)90375-0

http://dx.doi.org/10.1093/eurheartj/9.suppl_E.57

http://dx.doi.org/10.1016/S0002-9149(96)00235-4

http://dx.doi.org/10.1161/01.CIR.98.18.1949

http://dx.doi.org/10.1093/oxfordjournals.eurheartj.a015209

http://dx.doi.org/10.1161/01.CIR.95.10.2395


http://dx.doi.org/10.1161/01.CIR.66.5.1105


http://dx.doi.org/10.1378/chest.113.2.482

http://dx.doi.org/10.1016/S0003-4975(10)61452-X


http://dx.doi.org/10.1136/hrt.41.4.463

http://dx.doi.org/10.1161/01.CIR.101.16.1940

http://dx.doi.org/10.1016/0003-4975(95)00075-V


http://dx.doi.org/10.1016/0003-4975(90)90095-N


http://dx.doi.org/10.1016/S0735-1097(02)02002-8

http://dx.doi.org/10.1016/j.athoracsur.2007.02.094

http://dx.doi.org/10.1016/j.athoracsur.2006.07.048

### ABBREVIATIONS

AS: Aortic stenosis  
AVR: Aortic valve replacement  
NYHA: New York Heart Association  
PH: Pulmonary hypertension