

# Operative Treatment of Combined Aortic Stenosis and Coronary Artery Disease

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## ABSTRACT

**Introduction:** The aortic valve replacement is a standard operating procedure in patients with severe aortic stenosis. Structure of patients undergoing surgery ranges from young population with isolated mitral valvular disease to the elderly population, which is in addition to the underlying disease additionally burdened with comorbidity. One of the most commonly present factors that further complicate the surgery is coronary heart disease that occurs in, almost, one third of patients with aortic stenosis. The aim is to compare the results of surgery for aortic valve replacement with or without coronary artery bypass graft (CABG). **Patients and Methods:** From August 2008 to January 2013 in our center operated on 120 patients for aortic stenosis. Of this number, 75 were men and 45 women. The average age was 63.37 years (16-78). Isolated aortic valve replacement was performed in 89 patients and in 31 patients underwent aortic valve replacement and coronary bypass surgery. Implanted 89 biological and 31 mechanical valves. **Results:** Patients with associated aortic stenosis and coronary artery disease were more expressed symptomatic symptoms preoperatively to patients with isolated aortic stenosis who were on average younger age. Intra-hospital morbidity and mortality was more pronounced in the group of patients with concomitant aortic valve replacement and coronary bypass surgery. Morbidity was recorded in 17 patients (14.3%) in both groups, while the mortality rate in both groups was 12 patients (10.1%). **Conclusion:** Evaluation of preoperative risk factors and comorbidity in patients with aortic stenosis and coronary artery disease contributes to a significant reduction in intraoperative and postoperative complications. Also, early diagnosis of associated coronary artery disease and aortic stenosis contributes to timely decision for surgery thus avoiding subsequent ischaemic changes and myocardial damage.

**Key words:** Aortic stenosis, coronary artery disease, operative treatment.

## 1. INTRODUCTION

Aortic valve replacement (AVR) is the standard surgical treatment in patients with severe aortic stenosis (AS). Structure of patients undergoing surgery, ranging from young population with isolated mitral valvular disease to the elderly population, which is in addition to the underlying disease additionally burdened with comorbidity (1). One of the most commonly present factors that further complicate the surgery is coronary artery disease (CAD) that occurs in nearly one third of patients with AS. Untreated symptomatic AS reduces survival, and mortality within 5 years in patients with angina expressed about 50%. For AS associated with heart failure survival rate is less than two years (2, 3, 4, 5, 6).

## 2. PATIENTS AND METHODS

In the period August 2008–January 2013 at the Center for Heart BH operated on 119 patients for AS (area  $\leq 1\text{cm}^2$  TTE) with or without CABG. All patients underwent preoperative coronary angiography, echocardiography trans-thoracic (TTE) and transesophageal echocardiography

(TEE). The average age was 63.37 years and the female / male ratio was 45/74. Coronary artery disease (CAD) is defined by the presence of stenosis greater than 50% in at least one epicardial artery. Isolated AVR was performed in 88 patients, and in 31 patients with AVR and CABG done. All surgical procedures were performed in a standard way by median sternotomy using moderate systemic hypothermia (35 ° C). Myocardial protection was done crystalloid hyperkalemic solution mixed with the blood in the ratio 3: 2, antegrade and retrograde through the coronary sinus. Incorporated to the artificial valve, biological and mechanical, Sorin Biomedica St. Jude and Hancock. All patients were evaluated for postoperative anticoagulation Aspirin 300 mg for biological and Warfarin for mechanical valve and daily control levels of INR (International normalized ratio).

## 3. RESULTS

The average age of the entire study group was  $63.36 \pm 10.10$  years. Kolmogorov-Smirnov test for normality of distribution for the variable age is significant and speaks

Parameter:	Value	
Gender: Male-Female	n, (%)	74/45 (62.18% / 37.82%)
Age	± SD	63.36 ± 10.10
Valvular disease:		
AS	n, (%)	53 (44.54%)
AR	n, (%)	11 (9.24%)
AS+AR	n, (%)	55 (46.22%)
Isolated congenital heart disease	n, (%)	113 (94.96%)
Combined heart disease	n, (%)	6 (5.04%)
Operative treatment		
Single valve	n, (%)	113 (94.96%)
Two valve	n, (%)	6 (5.04%)
AVR	n, (%)	88 (73.95%)
AVR+CABG	n, (%)	31 (26.05%)
The outcome (alive/ex-letalis)	n, (%)	107 / 12 (89.92% / 10.08%)

Legend: n-absolute number and as a percentage. AS-aortic stenosis; AR-aortic regurgitation; AVR-aortic valve replacement. CABG-coronary artery disease.

**Table 1. Baseline characteristics of the sample (n=119).**

CABG		n	Valvular disease			Total
			AS	AS+AR	AR	
Coro- nary disease	Single vessel	n	5	5	1	11
	Two vessel	n	6	5	1	12
	Three vessel	n	7	1	0	8
	Total	n	18	11	2	31

Legend: Parameters were expressed as absolute number -n. Hi kvadrat test: Pearson Chi Square = 3.95, p=0.412. Cramer's V 0.252. Fisher's exact = 0.389

**Table 2. Valvular and associated coronary heart disease.**

negatively about asymmetrical distribution (-1.54 Skewness, Kurtosis 6.91). The youngest participant was 16 years old and the oldest 78 years. Since not fulfilled for parametric analysis, we conducted a nonparametric test variable age. The analysis of the age distribution by category type of valvular disease (AS, AR, AS + AR) we see that the pattern differed significantly in this parameter. The youngest patients, mean age 49.8 years, had severe AR as valvular defect with indication for operative treatment. Kruskal-Wallis equality-of-populations rank test,  $\chi^2 = 10.91$ ,  $df=2$ ,  $p = 0.004$  (Table 1).

We examined the difference in age by category type of heart disease (valvular defect or combined disease: cardiac valvular defect plus ischaemic heart disease). We see that the average age patients who underwent aortic valve replacement 62.2 years, and as expected, some elderly patients with a combination of valvular and ischaemic diseases. (Two-sample Wilcoxon rank-sum (Mann-Whitney) test,  $z = -3.06$ ,  $p = 0.002$ ).

Heart rhythm disorder by type of absolute dysrhythmia (Fibrillatio atriorum) had 17 (14.29%) patients, while the remaining 102 (85.71%) were free of cardiac arrhythmias. The proportion of cardiac arrhythmias by type AfibA. is similar although slightly more common in isolated valvular disease (vitium aortae) where observed in 14.77% cases. There was no statistical significance in the representation AfibA. Considering the type of surgical treat-

ment (Chi Square Pearson Chi Square (Yates' Correction for Continuity)  $\chi^2 = 0.065$ ,  $df=2$ ,  $p = 0.798$ , Cramer's V -0.0234. Fisher's exact = 1.0).

By type of prosthetic valve we see that the biological valve was the most common material installation, but there was no difference in relation to the type of surgical treatment. In six cases been replaced by two valves in patients who have had a combined heart defect (vitium aortic-mitral), which in addition had associated ischaemic (coronary) disease, so it was purely about valvular heart disease with normal angiogram. When the coronary disease was associated valvular always worked in isolated cardiac defect (vitium aortae) (Table 3).

Of the 31 patients with concomitant coronary artery disease, a three-pronged disease had 8 patients associated mainly with severe aortic stenosis. Due to the small number of cases undermines assumptions Chi-square test of independence was used Fisher's exact test probabilities for small samples, Fisher's exact  $p = 0.389$  here is not statistically significant (Chi Square, Fisher's exact  $p = 0.389$ , Pearson Chi Square  $\chi^2 = 3.95$ ,  $df = 2$ ,  $p = 0.412$ , Cramer's in 0.252).

Without hypertension was 30.25% of the patients while the other almost  $\approx 70\%$  were patients with high blood pressure. We observed that the proportion of hypertension similar in both operative treatment. Expected hypertension more common in the combination-ischemic valvular disease in 83.87%. A similar proportion of hypertension and isolated valvular diseases 64.77%. Chi-square test of independence showed us significant association between hypertension and operative treatment, (Pearson Chi Square = 3.95,  $p = 0.047$ . Cramer's V 0.18). However, given that the additional assumptions are not met Chi-

		n	Operative treatment		Total
			AVR	AVR+CABG	
Prosthetic valve	Biological	n	62	26	88
		%	70.45%	83.27%	73.95%
	Mehanical	n	26	5	31
		%	29.55%	16.13%	26.05%
Total	n	88	31	119	
	%	100%	100%	100%	

Legend: The parameters are expressed as n-absolute number and as a percentage a-Hi kvadrat test: Pearson Chi Square (Yates' Correction for Continuity)  $\chi^2 = 2.14$ ,  $df=1$ ,  $p=0.143$ . Cramer's V -0.0134.

**Table 3. Type of prosthetic valve and surgical treatment.**

square test of independence is recommended to use Fisher 'exact indication of probability' 'Fisher's exact = 0.068 who here did not reach statistical significance. Also, Effect size, ie. standard measure of strength of the relationship between variable) presented here Phi coefficient = 0.182 points us to a weak association to the reference Cohen's criterion (0.10-a small effect; 0.30-medium impact and 0.50-great impact).

The study is the proportion of chronic obstructive pulmonary disease in both operative treatment. Without COPD was 76.47% while the patient is 23:53% of patients with isolated valvular or combined disease had chronic obstructive pulmonary disease in comorbidity. The proportion is similar although slightly more common in the

Independent Samples Test(t-test for Equality of Means)							
Parameter	n	X	SD	p valule	Effect size Cohen's d	Mean Difference	95% CI: Low and Upp
OP-tretman							
AVA	88	63.68	0.70				
				0.0001	-2.13	-12.96	-15.5 -10.5
AVA+CABG	31	76.64	0.70				

Legend: Statistik t -10.24, df-117, Std.Error Difference 1.26, p<0.0001. Standardized mean difference Cohen's d -2.13, Point-Biserial r -0.75.

**Table 4. Total time of cardiopulmonary bypass by operating the treatment**

combination-ischemic valvular disease which is observed in 25.81% cases. (Chi-square test of independence did not show a significant relationship, Pearson Chi Square = 0.12, p = 0.728. Phi 0031, Fisher's exact = 0806).

We compared the proportion of diabetes mellitus (DM) in both operative treatment. Without diabetes was 72.88% of patients and 27.12% of patients with isolated or combined valvular disease and had associated diabetes. If we observe the observed frequencies, it can be seen that the proportion of DM frequent in the combined valvular-ischemic diseases where observed in 41.94% cases. (Chi-square test of independence showed us a significant relationship, Pearson Chi Square = 4.67, p = 0.031. Phi 0198, Fisher's exact = 0037). Tested and the proportion of stroke (CVI) in both operating treatment. Without CVI was most patients 92.44% of patients while is 7.56% of patients with isolated valvular or combined disease had and CVI. If we observe the observed frequencies, it can be seen that the proportion of CVI frequent in the combined valvular-ischemic diseases where noted in 19:35% cases. (Chi-square test: Pearson Chi Square  $\chi^2 = 8.33$ , df-1, p = 0.004. Phi 0264. Fisher's exact = 0009).

The outcome of our operations on a sample of 119 patients, including both operating treatment is encouraging, because 89.92% of our patients survived surgical treatment, while lethal hospital outcome was observed in 10.8% of cases, provided that no significant differences with regard to the type of operation. (Pearson Chi Square  $\chi^2 = 0.367$ , df-1, p = 0.544. Phi 0055. Fisher's exact = 0.508).

The average native valvular area (AVA) was  $0.69 \pm 0.15$  years. Shapiro-Wilk W test for normality of distribution for variable AVA is not significant and telling us about symmetrical distribution (12:28 Skewness, Kurtosis 0:09). Minimum AVA was 0,36 cm2 and maximum area of native valve which is subjected to an operative replacement was 1cm.2.

Test for independent samples, we compared the surface of native valvular patch with different operating treatments. The reported difference in surface between the operative treatment was negligible. Area native valve in isolated valvular disease was lower than in Area measured with combined disease, though the size effect (Effect size) presented Cohen's d coefficient indicates a small clinical implications of these differences.

The average duration of aortic cross-clamping amounted to  $48.67 \pm 4.93$  minutes. Shapiro-Wilk W test for normality of distribution for variable AoX time not significant and telling us about symmetrical distribution (00:37

Skewness, Kurtosis 0:13). Minimum time of aortic clamping was 39 minutes and a maximum of 62 minutes.

Test for independent samples, we compared the duration of clamping with different operating treatments. There was a significant difference in time between surgery treatments with important clinical implications. Search cross clamping of the aorta in the isolated valvular disease was significantly shorter with time clamping the aorta with combined disease, effect size (Effect size) presented Cohen's d coefficient indicates a large effect size of this

difference, the image x.

Since the valvular surgery demanding surgical technique supported cardiopulmonary bypass, a heart-lung machine (CPB), and the average duration of the extracorporeal circulatory support using a pump (CPB- cardiopulmonary bypass) amounted to  $67.05 \pm 8.31$  minutes. Shapiro-Wilk W test for normality of distribution for variable total CPB also not significant and telling us about symmetrical distribution (0.85 Skewness, Kurtosis 0002). Minimum time of extracorporeal circulation was 50 minutes and a maximum of 83 minutes (Table 4).

Test for independent samples were compared and the total duration of use " pump " with different operating treatments. There was a significant difference in time between surgery treatments with important clinical implications. Extracorporeal circulation time in isolated valvular disease was significantly shorter 63.68 min. in relation to the time of extracorporeal circulation combined with disease, the size of the effect (effect size) presented Cohen's d coefficient indicates a large effect size of this difference

In the Table 5, the most important postoperative complications in both operative treatment. Most of the operated patients (85.71%) had no significant complications. When referring observed cases, it can be seen that the CVI was recorded in 4 patients who had isolated valvular disease. The infection was observed in 8 patients (6.72%) cases, while major bleeding, perioperative myocardial in-

		Operative treatment		Total
		AVR	AVR+CABG	
Complications	No complications	n 77 % 87.50%	25 80.65%	102 85.71
	Bleeding	n 1 % 1.14%	1 3.23%	2 1.68%
	Infections	n 4 % 4.55%	4 12.90%	8 6.72%
	Peri-OP IM	n 1 % 1.14%	1 3.23%	2 1.68%
	Stroke	n 4 % 4.45%	0	4 3.36%
	ARI	n 1 % 1.14%	0	1 0.84%
	Total	n 88 % 100%	31 100%	119 100%

Legenda: Peri - OP - MI (peri operative IM). ARI-acute renal insufficiency. The parameters are expressed as n-absolute number. Hi kvadrat: Pearson Chi Square  $\chi^2 = 5.46$ , df-6, p=0.352. Cramer's V 0.214. Fisher's exact = 0.273.

**Table 5. Complications and surgical treatment.**

farction and acute renal failure (ARF) is a rare, individual cases. Chi-square test: Pearson Chi Square  $\chi^2 = 5.46$ , df-6,  $p = 0.352$ . Cramer's V 0.214. Fisher's exact = 0.273.

#### 4. DISCUSSION

In the presented study we have observed 119 patients divided into two groups, who had undergone AVR with or without CABG. There has been an increased morbidity and mortality in a group of patients with combined disease as a result of preexisting ischaemic myocardium, older age, and significant preoperative comorbidities. Most patients in this group according to NYHA classification belonged to the third and fourth degree (7, 8, 9). It was also noted that the patients from the group with combined disease were subjected to long-term CPB, and therefore larger ischaemic time. It is therefore important that such patients, with concomitant coronary disease and aortic stenosis, suggest surgery before the onset of myocardial damage caused by prolonged ischemia. In isolated AS because of chronic illness and left ventricular hypertrophy (LVH), there are some with myocardial protection and remodeling, resulting in increased, morbidity and mortality in the postoperative period (10). The patients, who were diagnosed with severe aortic stenosis and left ventricular hypertrophy, it is not necessary to delay surgery, even if symptoms are not very pronounced, as they are good candidates for early aortic valve replacement (11, 12). Consequently, the aim of this study was to show the importance of early diagnosis of the problem, because in our conditions unnecessarily long patients are treated conservatively. This can sometimes be very controversial because it is the biggest dilemma when operated on a patient? Then when the symptoms expressed, and echocardiographic findings showed moderate aortic valve stenosis, or when we have echocardiographic confirmation of severe aortic stenosis, but without symptoms (13, 14).

#### 5. CONCLUSION

Evaluation of preoperative risk factors and comorbidity in patients with aortic stenosis and coronary artery disease contributes to a significant reduction in intraoperative and postoperative complications. Also, early diagnosis of associated coronary artery disease and aortic stenosis contributes to timely decision for surgery thus avoiding subsequent ischaemic changes and myocardial damage. Combined aortic valve replacement and coronary artery bypass grafting is appropriate in the coexisting disease. Complete assessment of patient characteristics should be incorporated into the decision-making process.

**CONFLICT OF INTEREST: NONE DECLARED.**

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