

## FACTOR ASSOCIATE WITH MORTALITY RATE AFTER BALLOON AORTIC VALVULOPLASTY INOPERABLE PATIENTS WITH SEVERE AORTIC STENOSIS WITHOUT SUPPORT OF TRANSCATHETER AORTIC VALVULAR IMPLEMENTATION

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### ABSTRACT

**Aim/objectives:** Aortic balloon valvuloplasty (BAV) is a therapeutic option for some patients who are at high risk of transcatheter aortic replacement or surgical valve replacement and have severe aortic stenosis. In our research we examined survival and prognostic predictors in patients undergoing BAV with severe aortic stenosis. **Methods:** The study was conducted at the University Clinical Center of the Republic of Srpska. Patients diagnosed with severe aortic stenosis with high-risk for surgical replacement of the aortic valve, on which are preformed BAV procedure, after the decision made by the council of interventional cardiologists, were consider eligible candidate. **Results:** Patients (n=23) undergoing BAV procedure are elderly (mean age 80.9 years; minimum age 67 and maximum 92). There were 15 women (65.2%), and 8 men (34.8%). Total mortality after 1, 6 and 12 months was retrospectively 17%/27%/45%. The average survival was 14.1 months. The statistically significant predictors for one month survival were NYHA class and urgency of procedure. Hemodynamic parameters became better after the procedure, with statistically significant drop comparing to same parameters before procedure. **Conclusion:** Balloon aortic valvuloplasty is a relatively simple procedure, and the modern approach to it is as a rescue procedure and to give a window for patients to have better hemodynamic parameters and clinicians to prepare itself and patient for TAVR procedure.

**KEYWORD:** balloon aortic valvuloplasty; survival rate; transcatheter aortic valve replacement.

### INTRODUCTION

Ballon aortic valvuloplasty (BAV) was first performed by the team led by Cribier in 1986, in patients with severe aortic stenosis who were not suitable for surgical replacement of the aortic valve.<sup>[1]</sup> The first published results of 92 patient on which these procedures were performed, were very encouraging; the maximum transaortic gradient dropped from 75±26 mmHg to 30±13 mmHg, and aortic opening widened from 0.49±0.17 cm<sup>2</sup> to 0.93±0.36 cm<sup>2</sup>.<sup>[2]</sup> Based on this early findings authors suggested that this method of aortic valvular dilatation with balloon could be a simple alternative to surgical replacement of the aortic valve in elderly patients with high periprocedural risk.

However, restenosis and recurrence of symptoms were

common after 6 months and 1 year, and overall mortality after BAV was similar comparing it with untreated patients.<sup>[3]</sup> Although, findings from published researches suggested high risk of procedure itself, they also present significant but short-term clinical improvement, which follows poor clinical conditions.<sup>[4,5]</sup> Since the transcatheter aortic valve replacement (TAVR) had been introduce in therapy, the interest for BAV has been renew and even upgraded. In United States data shows that utilization of BAV procedure increased rapidly in last two decades, because balloon valvuloplasty allowed sufficient stabilization of the clinical condition and give patients the necessary time while they waiting for TAVR.<sup>[6]</sup>

Most important objective parameters that could evaluate the BAV efficiency could be obtained from noninvasive

echocardiography and includes changes in pre- and post-procedure transvalvular pressure gradients and effective aortic opening.<sup>[7,8]</sup> The results of a large registry, including 674 patients who underwent balloon valvuloplasty, found that the transvalvular gradient dropped by half immediately after the procedure and that the effective aortic opening increased by approximately 65%, but usually did not exceed 1 cm<sup>3</sup>. The stenosis increases again in the following months, and restenosis can also occur with few days or weeks after the procedure, which is the reason that some operators suggested a repeated procedure.<sup>[9]</sup> In addition to this suggestion, there is reports of 1-year survival of 58% for patients who had a single procedure, comparing to 84% of those patients who had a multiple valvuloplastic procedure.<sup>[10]</sup>

In borderline patient with poor left ventricular systolic function, chronic obstructive pulmonary disease (COPD), advanced comorbidities which are high-risk group of patients for TAVR procedure BAV procedure can be used as diagnostic tool. Also, except as bridge for TAVR in hemodynamically unstable patients, BAV can be consider as method of choice in other conditions such as bridge to urgent or high-risk noncardiac surgery, critically ill patients who are not candidates for TAVR, in palliative care, in congenital aortic stenosis and an adjunct to TAVR.<sup>[11]</sup>

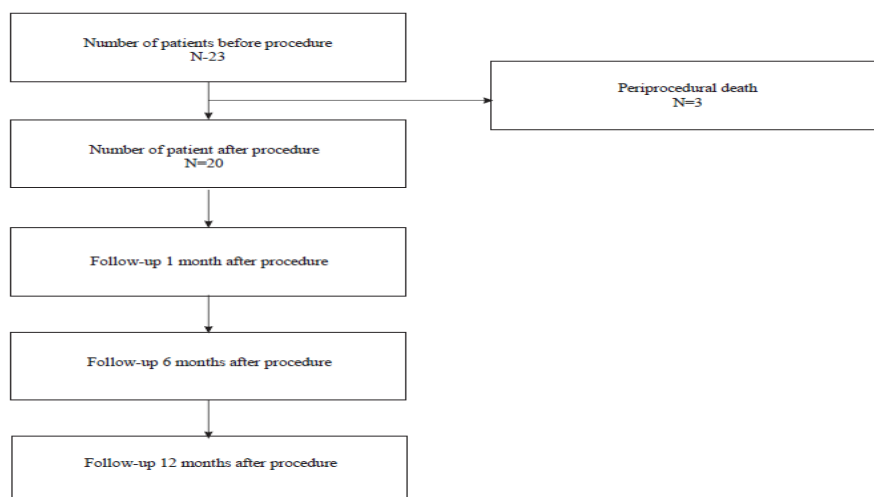
No matter what was the reason for balloon aortic valvuloplasty, procedures benefits and risk should be present to the patients. Risk includes vascular damage that may require surgical intervention (including hematomas, hemorrhages, pseudoaneurysms, dissections and vascular ischemia), myocardial infarctions, cerebral ischemia, ventricular perforation, tamponade, dysrhythmias, aortic dissection or in the worst-case scenario death.<sup>[11]</sup> Over the years, technological advances significantly improved the safety of the BAV, which is commensurate with the decline in the number of serious vascular complications from 13.5% in the 1990s to 4.6-7% as currently observed.<sup>[5,9]</sup> As a result, periprocedural

mortality is only about 1-5.6%, but the rates increase in the long-term monitoring. Long-term monitoring estimate that survival rate drops down from 50-68% after 6 months, 33-64% after 1 year and 18-37% after 3 years in patients that had only BAV procedure.<sup>[12,13]</sup> On the other hand, 50% of patients with symptomatically severe aortic stenosis treated pharmacologically die within 2 years of observation.

In our study we try to evaluate patients with severe aortic stenosis who were not candidates for surgical replacement of the aortic valve so therefore the balloon aortic valvuloplasty were performed. Also, we monitor these patients after the procedure and calculate mortality rate at different time period (1-month; 6-months; 12-months).

## METHODS

The study was conducted at the University Clinical Center of the Republic of Srpska between 2017-2021. Patients diagnosed with severe aortic stenosis with high-risk for surgical replacement of the aortic valve, on which are preformed BAV procedure, after the decision made by the council of interventional cardiologists, were consider eligible candidate. All valvuloplasty were performed percutaneously through the transfemoral aortic approach. Rapid ventricular pacing via transfemoral venous approach preformed as a support in all procedures. Therapeutic anticoagulation in the procedure were standard unfractionated heparin in dose of 70-100 IU/kg, and all the procedure were classified as elective or urgent. All the participants (patients) give the permission for the using necessary personal information and data for the purpose of this study. Data on echocardiographic findings before and after the intervention as well as on the long-term outcome of the disease were found in the information system of the University Clinical Center of the Republic of Srpska, and the other information considering monitoring of the participants were collected on regular follow-ups by the participants themselves or their guardians or relatives.



Picture 1: Organizational chart of the research.

**Statistical analysis**

Basic characteristic are presented as frequencies and percentages for categorical data, and as mean ± standard deviations for numerical data. Comparison between groups were shown using a two- sample t-test. The binary logistic regression model for mortality was designed to identify predictors of survival, relaying on gender, age, hypertension, ischemic heart disease, atrial fibrillation, chronic renal failure, diabetes, and other variables which examine this study. Pearson Chi-Square test was use for association between two categorical variables.

**RESULTS**

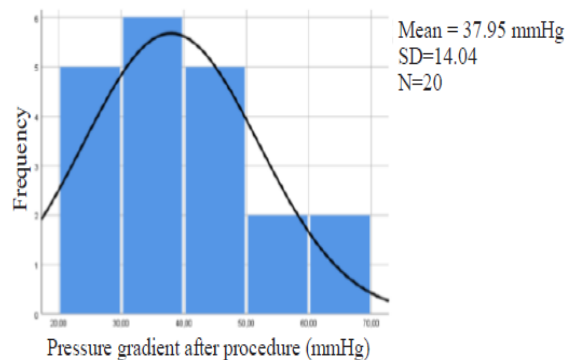
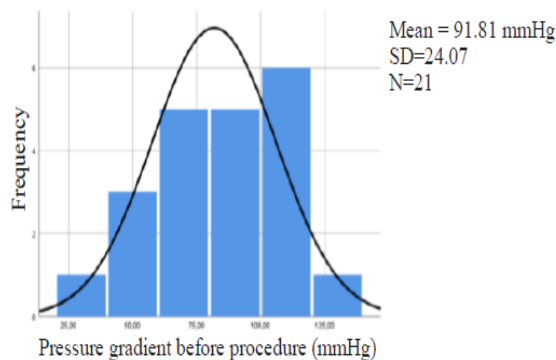
23 patients involved in the study, 8 (34.8%) of them were male, and 15 (65.2%) were women. The mean age was 80.9±5.6 (min. 67, max. 92), and the male participants were slightly older than the female (81.1 years old for male, comparing to the 80.8 years old for female). The basic demographic characteristics of the participants were shown in table 1.

**Table 1: Basic demographic characteristics of the participants.**

Characteristics	Value
Number of participants	23
Male	8 (34.8%)
Female	15 (65.2%)
Age	80.9±5.6

<b>Comorbidities</b>	
Diabetes mellitus	5 (21.7%)
Ischemic heart disease	19 (82.6%)
Chronic renal failure	8 (34.8%)
Atrial fibrillation	8 (34.8%)
<b>Type of procedure</b>	
Urgent	6 (26.1%)
Elective	17 (73.9%)

The mean value of the peak systolic pressure before procedure was 81.8 mmHg (39-116 mmHg). After the procedure were performed there were statistically significant drop in mean systolic pressure on 37.95 mmHg (20-68 mmHg, p<0.01, as it shown in Graph 1.). Pearson correlation coefficient between these two variables is 0.76, p<0.01, so it shown strong correlation and that 76% of distribution of pressure gradient after the procedure is depend on pressure gradient before the procedure. Nevertheless, there was no statistical significance between pressure gradient and the survival rate (1-month, 6-month and 12-month survival) in binary logistic regression model, probably because of the small sample size due to the specific conditions of patients and the procedure itself which were necessary for enrolment in this research. Picture 2 present the changes in hemodynamic parameters before and after the procedure.



**Graph 1: Distribution of frequencies of pressure gradient before (left) and after (right) the balloon aortic valvuloplasty.**

Since the binary logistic regression shown no statistically significance when the multiple variables (gradient pressure, sex, emergency of procedure and NYHA symptoms), due to the research restriction and small

sample size, we preform Chi-square test for categorical variables. We examine the codependents of NYHA before the procedure and survival rate after 1, 6 and 12 months. The results are presented in table 2.

**Table 2: NYHA class symptoms dependents with survival rate after one, six and twelve months after procedure.**

Follow-up checks after	Chi-square test ( $\chi^2$ )	p
1 month	4.439	0.035
6 months	2.758	0.097
12 months	0.303	0.587

As we can see from the table survival rate one month after procedure statistically significant depend on NYHA class after procedure. Specifically, 100% of the participants with NYHA class 3 or 4 survived one month after the procedure. We can't see these in the 6- or 12-

months survivalrate.

The next step was to find does the urgency of the procedure effect the survival rate. Results are shown in table 3.

**Table 3: Statistical dependence of urgency of procedure and survival one, six or twelve months after the balloon aortic valvuloplasty.**

Follow-up checks after	Chi-square test ( $\chi^2$ )	p
1 month	13.719	<0.001
6 months	6.45	0.011
12 months	-0.285	0.202

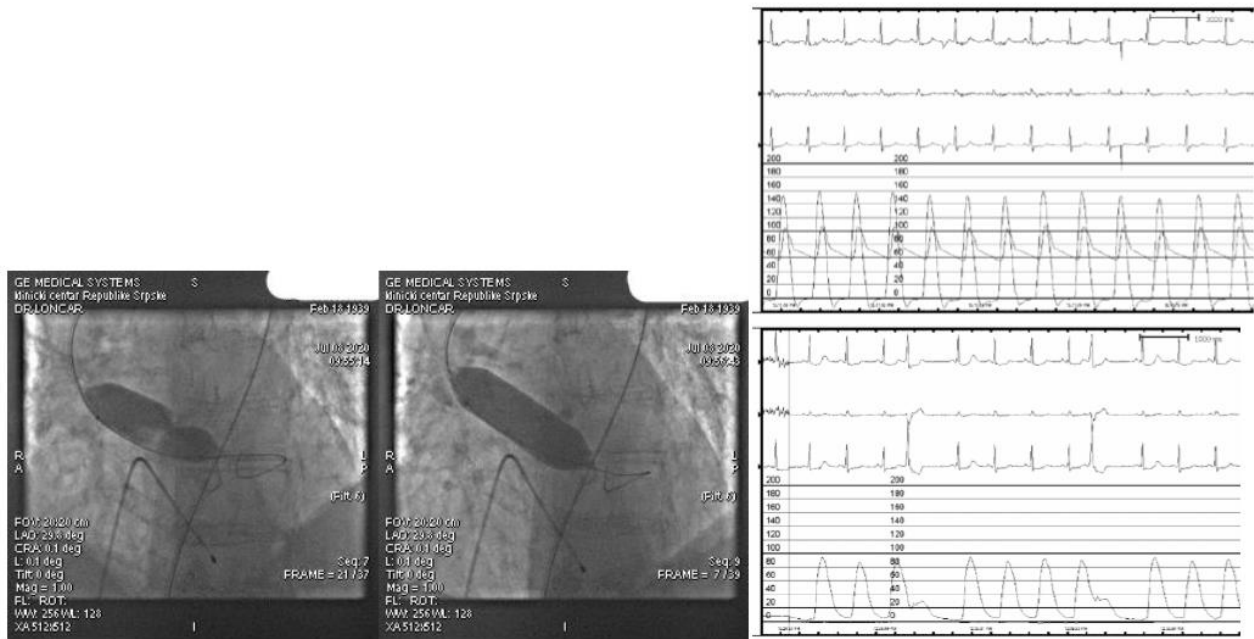
Survival rate strongly depends on urgency of procedure after one and six months, but have no statistical significance on survival rate twelve months after procedure. Results shows that after elective procedure 89.5% of participants were live after one month, and 87.5% after six months. Even there were no statistical significance between the survival rate and urgency of the procedure the results show that the average survival rate among the participants in our research were 14.1 months.

**DISCUSSION**

In this retrospective cohort study, we examined patients with severe aortic stenosis who were palliatively treated with balloon aortic valvuloplasty, and where not suitable

for transaortic valvule replacement. Our findings are correspondent with modern recommendations.

In the large IMPACT (Improving Pediatric and Adult Congenital Treatment Register), all BAV procedure performed from January 2011 and March 2015 are recorded, and it stated that BAV is an effective method for congenital aortic stenosis with a low mortality rate.<sup>[14]</sup> A total of 1126 patients were register, but due to incomplete data, only 1026 cases were processed and it was stated that in 70% of cases procedure was successful. On a significantly smaller sample, in our research, our results show even higher percentage of survival rate one month after the procedure.



**Picture 2: Hemodynamic parameters before (left and up) and after (right and down) the balloon aortic valvuloplasty, example of one participant.**

Although the surgical replacement of aortic valve is the cornerstone of therapy for patients with severe aortic stenosis today, and now this procedure is an acceptable standard for patients with symptomatic aortic stenosis who are not suitable for surgical treatment or who are not at high operative risk, the balloon aortic valvuloplasty still have the significant role. Patient who are not

candidate for neither of these procedures, due to the age, hemodynamic parameters or comorbidities, or patient on palliative care, treated with BAV got more time or even become suitable candidate for TAVR.<sup>[11]</sup>

PARTNER (Placement of Aortic Transcatheter Valves) study<sup>[15]</sup> which proved that one year mortality was

similar in patients treated with TAVR or surgical valve replacement proved that mortality after one year was similar in patients treated with TAVR or surgical valve replacement. Furthermore, it was published that there was no difference in survival rate or any other post treatment effect between these procedures, although the TAVR is less invasive than the surgical valve replacement.<sup>[16-18]</sup> Considering the BAV procedure just a step towards the TAVR, in our research we shown that the hemodynamic parameters are much better after the procedure and survival rate one month after the procedure was high enough that we can consider BAV procedure a step towards TAVR, and clinically this is less invasive method than the surgical valve replacement. Our findings suggest that we can give a minimum of one month period for patient to get better enough to be suitable for TAVR procedure, of the BAV procedure was elective and the patients before procedure had the NYHA class 3-4.

In the past few years, BAV procedure become again more interesting for bout clinicians and medical industry, as a step towards TAVR. Recent study shows that technical advance, considering the procedure itself, in this field have the positive effect on patients' mortality and morbidity.<sup>[19- 22]</sup> Furthermore, the one year survival of patients treated with BAV was similar with those treated with medication, but the patients treated with BAV have treated with BAV reported better quality of life comparing to those treated with medication.<sup>[23]</sup>

## CONCLUSION

Ballon aortic valvuloplasty is a relatively simple procedure associated with a rare complication. The modern approach to the treatment of patients with BAV in the transcatheter aortic valve replacement era has its place of application as a rescue procedure and to give a window for patients to have better hemodynamic parameters and clinicians to prepare itself and patient for TAVR procedure. The BAV lead to better quality of life in the period between two procedures, and improves short term mortality but doesn't change long term survival, if the TAVR procedure is not indicate. This strategy is an attractive form of treatment, but the application of it gains full capacity only as a bride to definitive percutaneous intervention therapy on the aortic valve, or TAVR.

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## Conflict of interest

The authors have declared no conflicts of interest.

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