Int Cardiovasc Res J.2018;**12**(3):105-109.icrj.56007

International Cardiovascular Research Journal

www.ircrj.com

Heart Function and Remodeling after Successful Balloon Valvuloplasty for Congenital Aortic Stenosis in Children

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ARTICLE INFO

Article Type:
Research Article

Article History:
Received: 23 Jun 2017
Revised: 30 Apr 2018
Accepted: 19 May 2018

Keywords:
Aortic Valve Stenosis
Balloon Valvuloplasty
Bicuspid Aortic Bicuspid Aortic Valve

ABSTRACT

Background: Congenital Aortic Stenosis (AS) is a common problem among congenital heart diseases and balloon valvuloplasty is known as the procedure of choice for treatment.

Objectives: This study aimed at evaluation of the function and remodeling of the heart after a successful balloon AS valvuloplasty.

Patients and Methods: From September 2012 to 2016, 33 patients with congenital AS who had successful balloon valvuloplasty were enrolled into this study. All patients were evaluated by 2D, M-mode, Doppler, and tissue Doppler echocardiography before and after the procedure. The data were analyzed using the SPSS statistical software.

Results: The median duration of follow-up was 2 years (range = 6 months to 7.4 years). Besides, the mean of immediate peak-to-peak gradient reduction was 41.50 ± 17.36 mmHg. Moderate to severe aortic insufficiency occurred in less than 28% of the patients. Additionally, M-mode echocardiography showed residual left ventricular hypertrophy in 50% of the patients. Moreover, E/A ratio was less than -2 Z-scores in 73% of the patients. E/Ea ratio was also more than 2 Z-scores in 50% of the patients, which was an indicator of diastolic dysfunction. The most common associated lesion was bicuspid aortic valve in 48% of the cases.

Conclusions: Balloon aortic valvuloplasty effectively reduced peak systolic pressure gradient across the aortic valve in patients with congenital AS although left ventricular hypertrophy and diastolic dysfunction persisted in a significant number of patients.

1. Background

Congenital Aortic Stenosis (AS) ranges from a mildly stenotic bicuspid valve without clinical symptoms to severe stenosis that can lead to hypoplastic left heart syndrome even in a fetus. AS accounts for 4 - 6% of congenital heart diseases with an incidence of 3.8 in 10000 births (less than 4 per 10000 based on a systematic review and meta-analysis) (1, 2). Congenital AS transpires in different forms and is usually classified into valvular, subvalvular, and supravalvular groups based on the location of the stenosis relative to the aortic valve. About 60 - 75% of all cases with congenital AS are valvular type (3-5) and it seems that males are affected more compared to females. Apart from symptomatic patients with infantile AS, most patients with congenital AS are asymptomatic during childhood. When the symptoms occur, fatigability, exertional dyspnea, angina pectoris, and syncope are the frequent manifestations (6, 7). However, normal growth and development are usually not affected.

Balloon valvuloplasty is the treatment of choice in patients with congenital AS. Yet, there is no treatment to stop the progression of aortic valve dysfunction. In contrast to adults with aortic stenosis, intervention is only recommended in children when symptoms develop or are considered

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imminent (8-13). In asymptomatic patients with severe congenital AS, relief of the obstruction is likely to reduce the risk of sudden cardiac death and diminish the extent of subtle and progressive myocardial injury as well as interstitial myocardial fibrosis (13-18). Even though surgical valvotomy may still be performed, balloon valvuloplasty has supplanted open surgical valvotomy as the initial treatment for congenital aortic valve stenosis in infants, children, and adolescents (13, 19-21).

2. Objectives

This study aims to evaluate heart function and regeneration after successful balloon valvuloplasty of aortic valve in children.

3. Patients and Methods

The proposal of the study was registered in the Research Committee of Shiraz University of Medical Sciences under certificate number 92-01-01-5597.

This study was conducted on 33 children under the age of 18 years who had successful balloon valvuloplasty in the hospitals affiliated to Shiraz University of Medical Sciences, Shiraz, Iran from 2012 to 2016.

In order for cardiac catheterization, conscious sedation without intubation was performed. Crossing the aortic valve from Ascending Aorta (AAO) to the left ventricle (LV) was done using a guide wire retrogradely and LV and AAO pressures were recorded before and after the procedure.

In order to perform balloon valvuloplasty, a balloon (Tyshak Mini and the Tyshak II NuMED, Hopkinton, NY or BALT) with approximate diameter of 80–90% (0.8 – 0.9:1 ratio) of the annulus of aorta was chosen.

3.1. Follow-up Echocardiography

Echocardiography was conducted with a GE vivid 3 system (GE Vingmed, Horten, Norway) using transducer 3 Mhz. All echocardiographic measurements were done by a pediatric cardiologist. Cardiac parameters were evaluated in order to raise intra-observer reliability. Echocardiographic studies included 2-dimensional, M-mode, Doppler, and tissue Doppler echocardiography. M-mode echocardiography involved measurement of the inter-ventricular septum, left ventricular posterior wall diameter in systole and diastole, ejection fraction, and fractional shortening in long-axis view. Besides, early diastolic inflow velocity (E), velocity during active atrial contraction (A), and E to A wave (E/A) ratio were measured by Doppler at the leaflets of the mitral (M) tips. Moreover, pulsed wave tissue Doppler velocities were collected at the cardiac base in the apical four-chamber orientation from two sites: the lateral mitral annulus and the inter-ventricular septum. Peak systolic annular velocity (S), peak early diastolic annular velocity (Ea), and peak late diastolic annular velocity (Aa) were collected, as well. All values were compared to normal values obtained from pediatric and fetal Z-score calculator website (22, 23).

3.2. Statistical Analysis

The study data were entered into the IBM SPSS Statistics for Windows, version 20 and were analyzed using descriptive statistics and Pearson's correlation coefficient. $P < 0.05$ was considered to be statistically significant.

4. Results

This study was performed on 33 patients between 0.5 months and 18 years old who had undergone balloon valvuloplasty for congenital AS. The median age of the patients at the time of balloon valvuloplasty was 2 years (range = 0.5 months to 18 years) and their median age during follow-up was 5.5 years (range = 6 months to 27 years). The median duration of follow-up was 2 years (range = 6 months to 7.4 years). During the follow-up, 9.4% of the patients were under 1 year old, 75% were 1 - 10 years old, and the remaining (15.6%) were 10-18 years old.

LV to aorta gradient was obtained before and after valvuloplasty. The mean peak to peak gradient was 61.65 ± 20.86 mmHg before and 20.15 ± 16.59 mmHg after balloon the procedure with the mean decrease of 40.50 ± 17.36 mmHg in the catheterization lab. During the follow-up period, LV to aortic peak instant gradient was 36.99 ± 16.65 mmHg.

Aortic annulus diameter Z-score was 0.79 ± 2.0. During the follow-up, annulus was less than -2 SD in 8% and more than 2 SD in 26% of the patients.

After balloon valvuloplasty, trivial, mild, moderate, and severe aortic insufficiency was detected in 12 (36.4%), 12 (36.4%), 8 (24.2%), and 1 patient (3%), respectively. In addition, mild (peek gradient < 40) and moderate (40 < peek gradient < 60) AS were found in 8 (24%) and 25 patients (76%), respectively. However, none of the cases showed severe AS.

Table 1. M-Mode Echocardiography Parameters and Their Z-Scores during Follow-up (N = 33)

	Mean ± SD (cm)	Percent of Patients with Z-Scores More Than 2	Percent of Patients with Z-Scores Less than -2	Z-Score ± SD
IVSD	2.40 ± 0.44	32.1	0	1.55 ± 1.06
IVSS	1.00 ± 0.35	29.6	0	1.31 ± 1.57
LVPWS	0.89 ± 0.31	29.6	0	-0.2 ± 1.64
LVPWD	0.72 ± 0.22	50	0	2.08 ± 1.19
LVIDD	3.52 ± 0.89	3.1	7.1	0.2 ± 1.39
LVIDS	1.91 ± 0.54	3.6	21.4	-0.93 ± 1.55
EF	77.72 ± 7.62			
SF	45.84 ± 7.66			

Abbreviations: IVSD, interventricular septum in diastole; IVSS, interventricular septum in systole; LVPWS, left ventricle posterior wall in systole; LVPWD, left ventricle posterior wall in diastole; LVIDD, left ventricle internal diameter in diastole; LVIDS, left ventricle internal diameter in systole; EF, ejection fraction; SF, shortening fraction

M-mode echocardiography showed that the Z-score of the Left Ventricular Posterior Wall Diameter (LVPWD) was more than 2 SD, but the Z-scores of other parameters were between -2 and 2. M-mode parameters and their Z-scores have been presented in Table 1.

Doppler echocardiography showed that the mean A wave velocity was more than 2 Z-scores and more than 60% of the patients had Z-scores > 2. Doppler parameters and their Z-scores have been depicted in Table 2. E to A (E/A) ratio was less than -2 Z-scores in 73% of the patients, but the mean was less than 10. Moreover, pulsed tissue Doppler study showed that the Z-scores of all parameters were between -2 and 2 (Table 3).

According to the follow-up echocardiography, residual aortic gradient (mean instant gradient: 36.99 ± 16.65) showed a positive weak correlation with the Z-scores of Left Ventricular Internal Diameter in Diastole (LVIDD;P = 0.001, r = 0.58), LVPWD (P = 0.004, r = 0.5), End Diastolic Volume (EDV; P = 0.001, r = 0.59), Interventricular Septum in Systole (IVSS; P = 0.005, r = 0.5), Left Ventricle Internal Diameter in systole (LVIDs; P = 0.008, r = 0.47), Left Ventricular Posterior Wall in systole (LVPWs; P = 0.002, r = 0.54), Systolic Volume (SV; P < 0.001, r = 0.6), and Septal Systolic motion velocity (Ss; P = 0.033, r = 0.39). However, it had no significant correlations with age at balloon valvuloplasty (P = 0.3 r = 0.41).

Echocardiographic and angiographic parameters were compared before and after valvuloplasty using Pearson's correlation coefficient, which showed no significant correlations in this respect. Moreover, 16 patients (48%) had Bicuspid Aortic Valve (BAV) in addition to AS. Indeed, BAV was significantly correlated to Ss (P = 0.023, r = 0.52).

5. Discussion

The present study results indicated that balloon valvuloplasty resulted in immediate hemodynamic improvement by decreasing trans-aortic pressure gradient, which remained stable during follow-up. The results showed that balloon aortic valvuloplasty could effectively relieve aortic valve stenosis in patients with moderate to severe congenital valvular stenosis. In fact, balloon valvuloplasty caused a 40-mmHg decrease in the mean aortic gradient. If we describe 40 mmHg reduction in aortic gradient as the cut-off point, nearly 76% of our patients reached this goal in comparison to 80% in another study performed on 90 patients (24). In our study, age, weight, aortic annulus diameter, severity of AS, and the presence of BAV did not influence the immediate reduction of aortoventricular pressure gradient.

After the procedure, no complication was observed, except for aortic regurgitation. The incidence rate of moderate aortic regurgitation was 24% during follow-up, which is a little lower compared to previous researches (33 - 38% in the studies by Lababidi et al. and Moore et al. and 33% in the BAV group in the study by Petit et al.) (25-27). Severe aortic regurgitation occurred in only one patient (3%) who had BAV, as well. The study results revealed no significant correlations between age and aortic regurgitation, which is in contrast to other studies that reported age as a risk factor for aortic regurgitation after angioplasty (26).

In the present study, more than half (50%) of the patients had residual Left Ventricular Hypertrophy (LVH) during follow-up (LVPWD > 2 Z-scores). This is similar to other studies, which reported 50% residual LVH or unchanged LV mass after Balloon valvuloplasty (24, 25, 28). LVH regression is probably multifactorial and depends on some other factors, such as time and age, which should be investigated in future studies.

In the current study, Doppler echocardiography showed that 70% of the patients had E/A ratio Z-scores < -2 (E/A ratio < 1), which indicated the persistence of diastolic dysfunction. In the same vein, Friedman et al. carried out a research on 25 patients who had undergone balloon valvuloplasty for congenital AS. In that study, left ventricular end-diastolic pressure was elevated in most

Table 2. Pulsed Doppler Echocardiography Parameters during Follow-up

	Mean ± SD (cm/s)	Z-score ± SD	Percent of Patients with Z-Scores Less than -2	Percent of Patients with Z-Scores More than 2
E Cm/S	124.64 ± 38.07	-0.48 ± 2.23	15	29
A Cm/S	92.59 ± 34.40	2.36 ± 1.12	0	60
E/ / A	1.42 ± 0.39	-1.84 ± 0.6	73	0

Abbreviations: E, early diastolic velocity of mitral valve; A, late diastolic velocity of mitral valve

Table 3. Tissue Doppler Echocardiography Statistics

	Mean ± SD (cm/s)	Z-score	Percent of Patients with Z-Scores Less than -2	Percent of Patients with Z-Scores More than 2
SM	9.05 ± 2.93	0.29 ± 1.04	0	10
Eam	15.10 ± 4.42	-0.18 ± 1	3.2	10
Aam	8.63 ± 2.48	1.22 ± 1.42	0	23
Ss	8.40 ± 1.52	0.68 ± 1.04	0	10
Eas	12.55 ± 2.76	0.04 ± 1.45	6.5	10
Aas	8.02 ± 1.94	1.36 ± 1.25	0	33
E/ Eam	8.77 ± 4.00	1.66 ± 1.49	0	50

Abbreviations: SM, systolic velocity of lateral mitral annulus; Eam, early diastolic velocity of mitral valve; Aam, late diastolic velocity of mitral valve; Ss, systolic velocity of septum; Aas, late diastolic velocity of septum; Eas, early diastolic velocity of septum

patients. Besides, median AS gradient decreased from 63 to 30 mmHg. In the median follow-up of 11 months, left ventricular end-diastolic volume Z-score increased, left ventricular mass remained unchanged, and left ventricular mass to volume ratio decreased significantly. Additionally, mitral annular and septal Ea velocity increased and E/Ea ratio decreased after dilation (28). These findings are in contrast to those of the present study, which showed a more persistent course of LVH and diastolic dysfunction (70% E/A ratio < 1 and 50% E/Ea ratio > 2 Z-scores).

The current study findings showed that only 8% of the patients had annulus size less than -2 SD during follow-up. However, interestingly, 26% of the patients had annulus size more than 2 SD. Growth of aortic valve annulus after balloon valvuloplasty was also reported in the research by Mc Elhinney et al. They evaluated neonatal aortic balloon valvuloplasty and revealed a 54 ± 26 mmHg reduction in aortic pressure gradient. In nearly 100% of their patients with aortic valve Z-score < -1, this normalized within 2 years. Left ventricular dimension Z-scores of -5 to -7.5 also reached the normal Z-score within 1 - 2 years after successful balloon valvuloplasty. Younger age, higher pre- and post-balloon pressure gradient, and larger balloon to annulus diameter ratio were correlated to re-intervention free survival (29).

5.1. Conclusion

Balloon aortic valvuloplasty could effectively reduce the peak systolic pressure gradient across the aortic valve in patients with congenital AS. Indeed, a significant number of patients had residual LVH and diastolic dysfunction after successful balloon valvuloplasty, which required further follow-up.

Acknowledgements

There is no acknowledgement.

Authors' Contribution

Study concept and design: Hamid Amoozgar, Acquisition of data: Farid Shahrivar, Mohammad Borzoee, Gholamhossein Ajami, Mohammadreza Edraki, Nima Mehdizadegan, Kambiz Keshavarz, Hamid Mohammadi, Analysis and interpretation of data: Hamid Mohammadi, Drafting of the manuscript: Hamid Mohammadi, kambiz Keshavarz, Critical revision of the manuscript for important intellectual content: Hamid Mohammadi, kambiz Keshavarz, Statistical analysis: Hamid Mohammadi

Funding/Support

There is no funding/support.

Financial Disclosure

There is no financial disclosure.

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