

Aortic balloon valvuloplasty and mid-term results in newborns: a single center experience

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ABSTRACT

Background and objectives. Aortic balloon valvuloplasty (ABV) has become the first-line treatment for critical aortic valve stenosis in infants. We aimed to evaluate the short- and mid-term results of patients who underwent ABV during neonatal period, the factors affecting the success and complications of the procedure.

Methods. We retrospectively examined 65 patients who underwent ABV during the neonatal period between 1998 and 2017. All hospital records including cardiac catheterization reports, echocardiographic information, and angiographic views were reviewed.

Results. Forty five (69.2%) of the patients were male and mean follow-up was 6.2 ± 4.9 years (range: 6 months - 19 years). The mean age of the patients at the first ABV was 14.5 ± 10.6 days (range: 1-30 days) and body weight was 3.25 ± 0.6 kg (range: 1.5-4.8 kg). The peak systolic gradient measured during pre-valvuloplasty cardiac catheterization was 73.3 ± 22.7 mmHg (range: 30-142 mmHg), and it decreased to 29.2 ± 12.2 mmHg (range: 5-55 mm Hg) after the procedure. Valvuloplasty was successful in 59 (90.7%) patients. There was no more than mild aortic regurgitation in any patient before valvuloplasty. There was mild aortic regurgitation in 21 patients before the valvuloplasty. In the acute phase after valvuloplasty, 30 patients had mild, 15 had moderate and two had severe aortic regurgitation. There was a significant increase in the degree of aortic regurgitation related to valvuloplasty ($p < 0.05$). The most important complication of ABV was increased aortic regurgitation (26.2%). Another important complication was femoral artery occlusion; and was detected early after valvuloplasty (61.6%). There was no serious complication or death in the acute phase.

Conclusions. In newborns with valvular aortic stenosis, balloon valvuloplasty has become the first choice in many centers due to its high success rate, low mortality and morbidity, and increased clinical experience. Aortic regurgitation and femoral artery occlusion were the most important complications. Although reintervention for residual or recurrent aortic valve stenosis is common during the first year after valvuloplasty, these patients are able to reach advanced ages without the need for surgical intervention. Surgical valvotomy is a good alternative treatment for a small number of patients in whom valvuloplasty fails.

Key words: balloon valvuloplasty, aortic valve stenosis, complication.

Aortic balloon valvuloplasty (ABV) is the first-line treatment for neonatal critical or severe aortic stenosis in many centers. Many studies have shown that balloon valvuloplasty effectively reduces the valvular gradient in aortic valve stenosis and the rate of short-term restenosis is low.^{1,3} Especially in critically ill newborns, it is a palliative approach that can be applied with

lower morbidity and mortality compared with aortic valve surgery. However, it is not always possible to completely eliminate morbidity and mortality with interventional therapy. Aortic valve morphology, the severity of the stenosis, left ventricular structure and function and the degree of regurgitation after valvuloplasty are possible factors determining the outcome.^{1,2} The most common complication of valvuloplasty is the increase in aortic regurgitation. Although development of mild to moderate aortic regurgitation after valvuloplasty is frequently reported, severe regurgitation is rare.^{1,2}

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Received 20th February 2019, accepted 15th April 2019.

In this study, we evaluated the efficacy of valvuloplasty in newborns with aortic valve stenosis, complications, factors affecting the development of aortic regurgitation, and the necessity and outcome of repeat valvuloplasty or aortic valve replacement in follow-up. As our series cover babies smaller than or 30 days old it is different from most of the studies which also include babies more than one month old.

Material and Methods

We retrospectively reviewed the data of 65 newborns with a critical or severe aortic valve stenosis who underwent ABV during the first 30 days of life between 1998-2017. All hospital records of the patients, including physical examination findings, cardiac catheterization reports, echocardiography information, and angiographic views were reviewed. Patients who underwent first ABV after the first 30 days of life, patients with missing catheter measurements, or patients with congenital heart disease who were not eligible for biventricular repair were excluded from the study. Both angiographic and echocardiographic examinations were used to classify the aortic regurgitation associated with the procedure. Criteria defined by the American Echocardiography Society were used for echocardiographic classification; 1) absence of aortic regurgitation, 2) mild grade aortic regurgitation, 3) moderate grade aortic regurgitation, and 4) severe grade aortic regurgitation.⁴ Grade of aortic regurgitation is assessed by aortic root angiography before and after valvuloplasty and was graded at the time of the procedure based on Seller's criteria.^{5,6} Grade 1+ (mild): A small amount of contrast material enters the left ventricle in diastole; it is essentially cleared with each beat and never fills the entire ventricular chamber. Grade 2+ (moderate): contrast enters the left ventricle with each diastole resulting in faint opacification of the entire chamber. Grade 3+ (moderate to severe): The left ventricle is well opacified and equal in density with the ascending aorta. Grade 4+ (severe): Complete dense opacification of the left ventricle in one

beat and appears more densely opacified than the ascending aorta.

Aortic valve morphology was classified by echocardiography as monocuspid, bicuspid (functional or anatomic bicuspid) and tricuspid. The presence of endocardial fibroelastosis was assessed by echocardiography. Left ventricular systolic functions were classified according to ejection fraction and shortening fraction data. If the ejection fraction is below 30%, left ventricular systolic function is considered to be severely impaired, between 31-57% moderately impaired, and above 58% normal left ventricular function. The diameter of the aortic annulus was measured by two-dimensional echocardiography and angiography in the left ventricular mid-systolic phase. Valvuloplasty procedure was started with balloons with balloon diameter/annulus diameter ratio of 0.75-0.9. The procedure was continued with the balloon diameter/annulus diameter ratio of 1-1.2 maximum, taking into account the residual transvalvular gradient and the grade of aortic regurgitation and, if necessary, increasing the balloon diameter by 1 mm. Valvular aortic gradient was determined by echocardiography by measuring peak gradient and mean gradient with continuous flow Doppler. In addition, systolic valvular gradient was measured during catheterization. Cardiac catheterization was performed when transthoracic echocardiography revealed a mean gradient of ≥ 50 mmHg in the aortic valve, ST-T wave change in patients with gradient < 50 mm Hg, presence of left ventricular systolic dysfunction, and/or decreased antegrade flow in the aortic valve. The success criteria for aortic valvuloplasty was 30% reduction in systolic pressure gradient, gradient < 50 mm Hg in patients with normal cardiac output, decreased left ventricle end diastolic pressure, increased forward flow from the valve, termination of prostaglandin E1 treatment and valvuloplasty-associated moderate or less aortic regurgitation. In all patients with sheath insertion in the femoral artery regardless of the presence of pulse after the procedure, heparin infusion was continued

at the dose of 20 units/kg/hour for at least six hours. Heparin was used as an anticoagulant in the treatment of patients with disturbed circulation of the extremity after venous access. Fibrinolytic therapy (streptokinase or tissue plasminogen activator) was started in patients without femoral pulse after 6 hours of heparin infusion. The loading dose of heparin was 50 units/kg (intravenous), and the maintenance dose was 20 units/kg/hour. For streptokinase, the intravenous loading dose was 3000 units/kg, and the maintenance dose was 1500-2000 units/kg/hour. Tissue plasminogen activator infusion was continued at the dose of 0.2 mg/kg/hour for five hours. During heparinization, activated partial thromboplastin time value was kept between 60-80 seconds. If the fibrinogen level dropped below 100 mg/dl after streptokinase or tissue plasminogen activator treatment, patients were administered fresh frozen plasma (10 ml/kg). Patients with absent pulse and/or disrupted blood flow in the extremities underwent Doppler ultrasonography.

This study was approved by the ethics committee of our university (KA18/338 – 06/11/2018).

Statistical analysis: Statistical analysis was performed using the PASW version 17.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed in mean \pm standard deviation (SD), and frequency. A p value less than 0.05 was considered statistically significant.

Results

Diagnosis of aortic stenosis was based on auscultation of a cardiac murmur in 46 patients during a routine visit, 12 were diagnosed after cardiac examination due to respiratory distress and/or cyanosis, five were diagnosed during antenatal period and two were diagnosed after deterioration of the general condition and development of metabolic acidosis. Aortic valve morphology was monocuspid in four patients and bicuspid in 61. A total of 85 aortic balloon valvuloplasties were performed in 65 patients.

At the first valvuloplasty procedure, the mean age of the patients was 14.5 ± 10.6 days (1-30 days) and body weight was 3.25 ± 0.6 kg (1.5-4.8 kg). Before the valvuloplasty, the aortic valve annulus was 6.5 ± 0.9 mm (4-8.8 mm), z score was -0.53 ± 1.59 (-5.43 - 3.06), the mitral valve annulus was 11.1 ± 2 mm (6-15.7 mm), z score was -0.37 ± 1.18 (-4.39 - 2.05). The mean balloon diameter/annulus diameter ratio was 0.96 ± 0.1 (0.75-1.2) (Fig. 1) and the balloon diameter was 6.1 ± 0.6 mm (3.5-7 mm). The stenosis of the aortic valve was critical in 26 (40%) patients. Five patients underwent predilatation with 3.5-4 mm (2 cm length) coronary angioplasty balloons followed by dilatation with 5-6 mm (2 cm) valvuloplasty balloons. A patient with critical valvular aortic stenosis concomitant with aortic arch hypoplasia was dilated with a 3.5 mm (2 cm) coronary angioplasty balloon. In this patient, the procedure was not continued

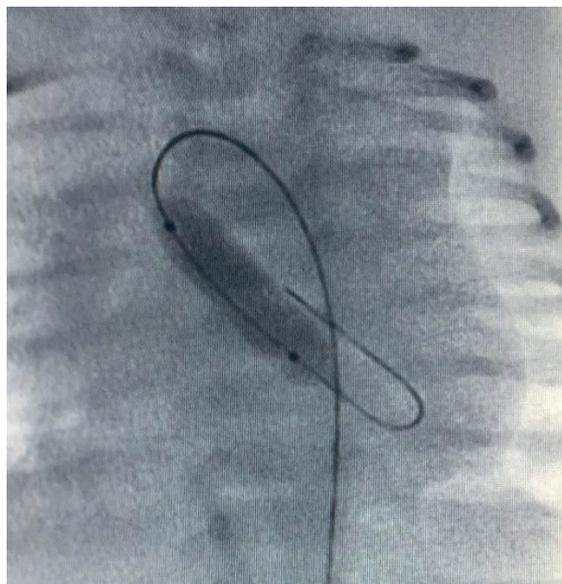


Fig. 1. The angiogram of a 6 day-old newborn with bicuspid aortic valve and severe valvular aortic stenosis. Aortic annulus was measured 6.5 mm. Balloon aortic valvuloplasty was performed by using 6 mm (2 cm) balloon (balloon diameter/annulus diameter: 0.92; Tyshak-II, NuMed Canada Inc., Cornwall, Canada). The peak systolic gradient in the aortic valve regressed from 98 mmHg to 32 mmHg; there was no aortic regurgitation in the aortogram performed after the procedure.

because the aortic annulus was 4 mm and hypoplastic aortic arch was present. Twenty (30.8%) of the patients also had stenosis in other left heart structures. The most common pathologies were aortic coarctation (21.5%), aortic arch hypoplasia (15.6%) and mitral valve stenosis (10.7%). Nine (13.8%) patients had multiple left-sided obstructive lesions in addition to aortic valve stenosis (Table I).

ABV was performed in all patients via femoral artery. In all patients with sheath insertion in the femoral artery regardless of pulse status after the procedure, heparin infusion was continued for at least six hours. Twenty four of 30 patients without palpable pulse received streptokinase, whereas six received TPA. No serious bleeding or circulatory disturbance in the extremities was observed during these treatments. Despite the anticoagulation treatment, there was no palpable femoral pulse in eight of these patients during discharge. There was no circulatory compromise in their extremities. Dysrhythmia developed in three patients during the procedure; supraventricular tachycardia which resolved with adenosine treatment occurred in one patient and spontaneously resolved nonsustained ventricular tachycardia occurred in two patients during the procedure.

The mean peak systolic gradient before and after the procedure, and the mean decrease in

the gradient is shown in (Table II). Eight patients (12.3%) had significant heart failure symptoms before the intervention. Seventeen (26.2%) patients received inotropic drug treatment for 8.1 ± 5.8 days (range: 3-23 days) and eight (12.3%) patients received prostaglandin E1 treatment for 3.2 ± 2.1 days (range: 1-7 days). There was no significant association between the decrease in the gradient and the final balloon diameter/annulus diameter ratio ($p >0.05$). Similarly, there was no significant association between the increase in aortic regurgitation degree and the final balloon diameter/annulus diameter ratio ($p >0.05$).

There was no significant association between aortic valve morphology and gradient determined before valvuloplasty, decrease in postoperative gradient and increase in aortic regurgitation degree ($p >0.05$). There was no significant association between aortic valve morphology and severity of aortic stenosis ($p >0.05$) and with the need for repeat ABV ($p >0.05$).

Thirty-eight (58.5%) patients had endocardial fibroelastosis. Endocardial fibroelastosis was present in 76.9% of patients with critical aortic stenosis and in 44.7% of patients with non-critical aortic stenosis. There was a significant association between critical aortic stenosis and endocardial fibroelastosis ($p <0.05$). Patients

Table I. Demographic and clinical characteristics of the patients (N=65).

Characteristics	Results
Female/male, n (%)	20 (30.8) / 45 (69.2)
Age, days	14.5 ± 10.6 (range: 1-30)
Body weight, kg	3.25 ± 0.6 (range: 1.5-4.8)
Follow-up time, years	6.2 ± 4.9
Aortic valve morphology, n (%)	
Bicuspid	61 (93.8)
Monocuspid	4 (6.2)
Aortic arch hypoplasia, n (%)	10 (15.6)
Mitral valve stenosis, n (%)	7 (10.7)
Multiple left-sided obstructive lesions, n (%)	9 (13.8)
Endocardial fibroelastosis, n (%)	38 (58.5)
Moderate left ventricular systolic dysfunction, n (%)	16 (24.6)
Severe left ventricular systolic dysfunction, n (%)	22 (33.8)

Table II. Data and complications related to aortic balloon valvuloplasty procedure.

Features	Results
Pre-ABV catheter peak systolic gradient, mmHg	73.3 ± 22.7 (range: 30-142)
Post-ABV catheter peak systolic gradient, mmHg	29.2 ± 12.2 (range: 5-55)
Decrease in the gradient, mmHg	44.1 ± 20.8 (range: 10-127)
Pre-ABV aortic valve annulus, mm	6.5 ± 0.9 (range: 4-8.8)
Balloon diameter, mm	6.1 ± 0.6 (range: 3.5-7)
Balloon diameter / annulus diameter ratio	0.96 ± 0.1 (range: 0.75-1.2)
Pre-ABV aortic regurgitation moderate and severe	None
Post-ABV aortic regurgitation moderate and severe, n (%)	17 (26.2)
Repeat ABV, n (%)	17 (26.2)
Surgical valvotomy, n (%)	4 (6.2)
Aortic valve replacement, n (%)	7 (10.7)
Ross procedure, n (%)	1 (1.5)
ABV success rate, n (%)	59 (90.7)
Femoral artery occlusion, n (%)	30 (46.2)
Dysrhythmia, n (%)	3 (4.6)

ABV: aortic balloon valvuloplasty

with endocardial fibroelastosis had decreased ejection fraction [$47.9 \pm 18.8\%$ (range: 18-76%) versus $68.8 \pm 11.7\%$ (range: 45-85%), $p < 0.05$] and shortening fraction value [$23.2 \pm 11\%$ (range: 8-42%) versus $36.9 \pm 9.1\%$ (range: 21-55%), ($p < 0.05$)].

There was no significant difference in the increase of aortic regurgitation degree related to valvuloplasty between the patients with critical aortic valve stenosis and the other patients ($p > 0.05$). Valvuloplasty was repeated at least once in 53.3% of patients with critical aortic valve stenosis and in 20.7% of other patients. The rate of repeat valvuloplasty in patients with critical aortic valve stenosis was significantly higher than the other patients ($p < 0.05$). Surgical intervention was performed in 15.4% of patients with critical aortic valve stenosis and in 15.4% of other patients. There was no significant difference between two groups for requirement of surgical intervention.

In 18.5% of the patients, surgical intervention was performed once to the aortic valve and in 6% of the patients a second operation was performed. In six patients, aortic valve replacement was performed due to severe aortic regurgitation.

Vegetation resection and aortic valve replacement was made in one patient due to infective endocarditis. Four patients underwent surgical valvotomy due to unsuccessful valvuloplasty, two patients underwent repeat surgical valvotomy due to recurrence of aortic valve stenosis, two patients underwent reoperation for aortic valve replacement due to prosthetic valve dysfunction, and one patient underwent Ross procedure. In addition, three patients underwent coarctation repair and one patient underwent repair of ascending aorta aneurysm. The first surgery was performed at a mean age of 3.1 ± 3.8 years (range: 26 days-10 years) and the second at a mean age of 10.5 ± 2.5 years (range: 8-14 years).

In patients with critical aortic valve disease, the mean ejection fraction was $44.9 \pm 20.6\%$ (range: 18-77%) and the mean shortening fraction was $21.7 \pm 11.9\%$ (range: 8-42%). In other patients, the mean ejection fraction was $65.2 \pm 13.5\%$ (range: 30-85%) and the mean shortening fraction was $34.1 \pm 9.7\%$ (range: 13-54%). In patients with critical aortic valve stenosis, both ejection fraction and shortening fraction values were significantly lower than the other patients ($p < 0.05$).

There was no significant difference in the annulus diameter, valve morphology, balloon diameter/annulus diameter ratio, aortic gradient, reduction in gradient with valvuloplasty procedure, and aortic annulus Z-score between patients with mild to moderate aortic regurgitation related to valvuloplasty and patients with severe aortic regurgitation related to valvuloplasty ($p > 0.05$).

In 14 patients with severe left ventricular systolic dysfunction (ejection fraction $\leq 30\%$ before valvuloplasty), complete recovery was achieved within the first six months after the procedure. Six patients died without improvement in the ejection fraction, no data were available for two patients. In 16 patients with moderate left ventricular systolic dysfunction (ejection fraction: 31-57% before valvuloplasty), complete recovery was achieved within the first six months after the procedure. Aortic regurgitation before valvuloplasty was mild in 32.8% of patients, and absent in 67.2%. Aortic regurgitation after valvuloplasty was mild in 46.9% of patients, moderate in 23.1% and severe in 3.1%. There was a significant increase in the degree of aortic regurgitation after valvuloplasty ($p < 0.05$). ABV was successful in 59 patients (90.7%). Surgical valvotomy was performed in two patients with critical aortic stenosis because the guidewire and catheter could not be advanced from the valve. Two patients underwent surgical valvotomy as there was no significant reduction in aortic gradient. The procedure was considered unsuccessful in two patients because severe aortic regurgitation developed early after the procedure. Femoral artery occlusion developed in 40 (61.5%) patients, increase in aortic regurgitation in 36 (55.3%), hematoma at the entrance site in one patient, respiratory depression requiring short duration respiratory support in one patient, and convulsion developed in one patient. In the late period, moderate dilatation of the ascending aorta developed in four patients and aneurysmatic dilatation requiring surgical repair was present in one patient. There was no serious complication or death associated with ABV procedure.

Seventeen patients developed re-stenosis during follow-up, second valvuloplasty was performed at a mean of 27.2 ± 45.8 months of age (range: 5 days - 13 years). In one patient, third valvuloplasty was performed at 16 months of age. Freedom from reintervention after valvuloplasty was 71.7% in the first year, 58.8% in the third year, 53.1% in the fifth year, and 26.9% in the tenth year of follow-up.

Six patients died in the first year. One died due to sepsis and multiorgan failure in the fifth day after valvuloplasty. One died due to low cardiac output and cardiac arrest in the early period after the Ross procedure and coarctation repair. The other four patients who died had Shone complex. None died during valvuloplasty. It was determined that all deceased patients had critical valvular aortic stenosis, severe left ventricular dysfunction and other stenotic lesions in left heart structures.

Discussion

Aortic balloon valvuloplasty in neonatal patients is safely performed as a first-line treatment in many centers around the world.^{2,7-9} Until the first half of 1980s, the standard treatment approach was surgical valvotomy. Lababidi et al.¹⁰ performed ABV for the first time in 1984. Subsequent studies have reported that ABV is an alternative and effective method to surgical valvotomy.^{1,2,11-13} In accordance with the literature, we determined that most patients were diagnosed with cardiac examination on the basis of murmur during routine examination. We have shown that ABV is an effective intervention to reduce the aortic valve gradient in patients with congenital aortic valve stenosis. Many similar studies have reported an effective reduction of the gradient with valvuloplasty and a low rate of restenosis in the early period.^{1-3,14,15} Sullivan et al.² reported that the most common lesion associated with aortic valve stenosis was aortic coarctation (21%) and mitral valve stenosis (7.8%). In this study, 5.8% of patients had multiple left-sided obstructive lesions in addition to aortic valve

stenosis. In accordance with the literature, the most common obstructive lesions associated with valvular aortic stenosis in our study were aortic coarctation, aortic arch hypoplasia and mitral valve stenosis.

Few studies have reported that ABV was performed with access through the femoral vein, umbilical artery or umbilical vein.^{2,14,16} As in our study, valvuloplasty was performed via femoral artery in many studies.

Sullivan et al.² reported that mean peak systolic gradient was 61 ± 23 mmHg before, and 18 ± 9 mmHg after valvuloplasty. The acute decrease in the gradient was 43 ± 21 mmHg. We also found that the residual gradient was at acceptable level after valvuloplasty. In our patients, valvuloplasty was successful at a high rate (90.7%). In six patients the procedure was considered unsuccessful. There was no significant decrease in aortic gradient in two patients. We failed to advance the guidewire through the valve in two and they underwent surgery. Severe aortic regurgitation developed in two patients after the procedure. Surgical valvotomy was performed successfully in four patients. Surgical valvotomy is a good treatment option for thick, dysplastic valves through which a guidewire can not be advanced.

Several complications related to ABV such as aortic regurgitation, femoral artery thrombosis, left ventricular perforation, pericardial tamponade, aortic perforation, excessive blood loss, life-threatening arrhythmia and death have been reported.^{1,2,11,17,18} Balloon valvuloplasty-related mortality is reported in critical aortic valve stenosis, severe left ventricular systolic dysfunction, or accompanying complex anomalies.^{19,20} In studies comparing surgical valvotomy with percutaneous valvuloplasty, early mortality rate in the surgical group is reported as 10-28.5% whereas it was 0-16.6% in the valvuloplasty group, although the long-term results of both procedures are similar.^{1,12,13} In recent years, early mortality related to surgical valvotomy in newborns has been reported at lower rates, but there are also reports giving

rates as high as 20-30% and this is extremely high.^{12,21} Torres et al.¹ reported no death because of valvuloplasty in their multicenter study. Sullivan et al.² also reported no death in 76 newborns. High mortality rates are reported in case of accompanying stenotic left heart pathologies.^{22,23} The mortality rate was 9.3% in our study. All of the patients who died had critical aortic stenosis, severe left ventricular dysfunction or had stenotic left heart lesions. In our study, the most important complications of ABV was increased aortic regurgitation and femoral artery occlusion. There was no serious complication or death associated with ABV.

Vascular injury or obstruction are the most common problems in these patients. Vascular complications are significantly reduced with anticoagulant and/or fibrinolytic treatment. We observed that anticoagulant and/or fibrinolytic drugs can be safely used in newborns for the treatment of obstruction in the femoral artery during interventional procedures.

Severe dysrhythmia related to valvuloplasty may be seen in patients with impaired left ventricular systolic function. Ventricular tachycardia, ventricular fibrillation, supraventricular tachycardia, and atrioventricular block are frequently reported. The incidence of dysrhythmia has been reported as 1-13% in different series.^{14,21} There was no serious dysrhythmia resulting in mortality or morbidity in our series.

The increase in valvuloplasty-associated aortic regurgitation was reported as 43% in the series of Labadibi, 7-59% in different studies.^{1,2,10,11} The incidence of moderate and severe aortic regurgitation was 2.2-29%.^{1-3,11,14} The development of aortic regurgitation after valvuloplasty in newborns is more frequent.^{2,14,24} Fratz et al.²⁴ reported that the incidence of moderate and severe aortic regurgitation after valvuloplasty was 29% in newborns and 19% in babies older than one months of age. Sullivan et al.² also reported that the incidence of moderate and severe aortic regurgitation after valvuloplasty was 16% in newborns and

9% in others. While the effect of large diameter balloons on aortic regurgitation in neonates is not yet clear, balloons with a final balloon/annulus diameter ratio of 0.9-1 have been used in many studies.^{2,8} Lewin et al.²⁶ reported that there was a significant correlation between frequency of moderate-severe aortic regurgitation and the ratio of balloon diameter/annulus diameter. However, Hamidi-Manesh et al.²⁵ showed that there was no significant correlation. Reich et al.¹⁷ reported that a functional bicuspid aortic valve is an independent risk factor for the appearance of aortic regurgitation after valvuloplasty. In our study, the aortic regurgitation related to valvuloplasty was moderate in 23.1% and severe in 3.1% of infants. There was no significant association between the increase in aortic regurgitation and the balloon diameter/annulus diameter ratio. This may be so because we kept the balloon diameter as low as possible. To prevent moderate-to-severe aortic regurgitation it is important to perform a careful measurement of the annulus diameter by both echocardiography and angiography, to initiate valvuloplasty with a smaller diameter balloon, to check for pressure and aortic regurgitation after each procedure and, if necessary, to use a larger diameter balloon. In order to choose the balloon diameter we use both echocardiographic and angiographic measurements. Considering a smaller measurement may be useful in reducing aortic regurgitation.

Endocardial fibroelastosis causes considerable volume and size loss with diastolic dysfunction in the left ventricle.^{3,27} Although biventricular repair can be performed in patients with borderline left ventricular structure¹⁹, there are studies reporting that this is an important risk factor for mortality.^{28,29} In our study, we determined left ventricular systolic dysfunction, borderline left ventricular structure and endocardial fibroelastosis as important risk factors for mortality.

Soulatges et al.³ reported freedom from surgical intervention and transcatheter intervention as 72.9% and 54%, respectively in 37 newborns at a mean follow-up of 11 years. Rossi et al.³⁰

also reported freedom from surgical and transcatheter intervention as 47% and 59%, respectively at a mean follow-up of 10 years. In many studies, freedom from reintervention (surgery or transcatheter) after valvuloplasty was reported as 40-60%.^{3,9,30-33} In our study, the results were similar to the literature. In accordance with previous studies, severe aortic regurgitation and recurrent aortic valve stenosis were the most important reasons for late surgical intervention in our series.^{2,24,27}

It has been reported that the presence of endocardial fibroelastosis in patients with congenital aortic valve stenosis causes left ventricular systolic and diastolic dysfunction and increased mortality.³⁴⁻³⁶ Same was true for our study. We determined that left ventricular systolic dysfunction was both more frequent and more severe in patients with critical aortic valve stenosis. The need for inotropic support and length of stay in hospital were significantly prolonged in patients with left ventricular systolic dysfunction after valvuloplasty.

The success of valvuloplasty was found to be associated with the diameter of the valve annulus.^{37,38} In our study, we found no association with annulus diameter, but there was an association between the need for reintervention and the diameter of the annulus in the mid-term follow-up. Many studies have reported that the duration of hospital stay after valvuloplasty was shorter, morbidity and mortality were less, but the need for reintervention was higher.^{19,21} In our series, the duration of hospital stay of patients undergoing valvuloplasty who had no additional cardiac pathology was very short.

Aortic valve replacement is required due to progressive severe aortic regurgitation during or after valvuloplasty.^{2,24} The incidence of severe aortic regurgitation in the long-term has been reported as 21-38%.^{2,39} Nine of our patients (13.8%) developed severe aortic regurgitation at follow-up. In six of them, aortic valve replacement was performed due to progressive increase in aortic regurgitation and left

ventricular dilatation. Three patients remained in follow-up. The data show that valvuloplasty has a low mortality risk in the mid- to long-term. However, it has significant risks such as valve dysfunction and aortic valve replacement in the long-term.^{2,9} Sullivan et al.² reported that aortic valve replacement was not required in 45% of newborns at 15 years of follow-up after ABV. Maskatia et al.⁹ also reported that aortic valve replacement was not required in 70% and 61% of patients at 10 and 15 years of follow-up after ABV, respectively. In our series, six patients (9.2%) underwent aortic valve replacement due to severe aortic regurgitation, one (1.5%) underwent Ross procedure and coarctation repair at a mean follow-up of 6.2 ± 4.9 years after valvuloplasty. In addition, five of these patients underwent Konno procedure and one patient underwent repair of ascending aorta aneurysm.

In many studies residual aortic stenosis and acute aortic regurgitation after valvuloplasty are found to be the most important risk factors for aortic valve replacement in the long-term.^{2,9,31} Therefore, it is very important to identify correctable risk factors determining long-term valve functions. Risk factors associated with aortic valve replacement should be considered when deciding whether to continue procedure in the residual aortic stenosis. In our study, we determined that the most important risk factor associated with aortic valve replacement was moderate-severe aortic regurgitation, which developed after the procedure and continued during the follow-up. We prefer to terminate the procedure in the gray zone of 40-50 mmHg gradient for residual aortic stenosis in order to avoid increase in the aortic regurgitation.

One of the most important problems for the operator is the persistence of high residual AS after valvuloplasty in case of dysplastic and thick valves. Should the procedure continue with larger balloons, with the risk of aortic regurgitation or should the procedure be terminated? Sullivan et al.² found that patients with moderate or severe acute aortic regurgitation and a residual AS gradient <30 mmHg after valvuloplasty had an approximately

three times greater risk of requiring AVR compared to those patients with a residual AS gradient ≥ 30 mmHg and mild or less aortic regurgitation. In addition, all patients with acute moderate or severe aortic regurgitation underwent aortic valve replacement at 15 years of follow-up while aortic valve replacement was not required in 52% of cases with high residual gradient and mild or less aortic regurgitation.² In our study, 45% of cases with residual gradient <40 mmHg in the acute period and moderate-severe aortic regurgitation underwent aortic valve replacement. On the other hand, aortic valve replacement was performed in 6.2% of cases with residual gradient ≥ 40 mmHg in the acute period and mild or no aortic regurgitation. However, we think that there is insufficient data to determine risk factors for aortic valve replacement and re-intervention types because the number of cases was low and the mean follow-up period was 6.2 ± 4.9 years. We believe that follow-up with tolerable residual aortic stenosis after valvuloplasty is better than severe acute post-valvuloplasty aortic regurgitation to avoid aortic valve replacement in the mid and long-term.

A retrospective study is a significant disadvantage in the collection and evaluation of data. The change of the pediatric cardiologist and the surgical team performing the interventional procedures during 18 years may have caused differences in patient selection and treatment strategy. At the same time, the progress in medical equipment technology during this period might have affected the results. The number of patients (65 newborns) was a significant advantage, but the number of patients undergoing surgical valvotomy was low and comparison of surgical valvotomy with balloon valvuloplasty was not possible.

In conclusion, the choice of valvuloplasty or surgical intervention in valvular aortic stenosis depends on the experience of the center. Recently, the initial treatment of choice in newborns is ABV because of the lower mortality. The prognosis of the patient is closely related to the left ventricular structure and the

development of aortic regurgitation. Although valvuloplasty is a safe and effective procedure in the treatment of congenital aortic stenosis, it should be known that it involves significant risks such as regurgitation, requirement for reintervention, and aortic valve replacement.

REFERENCES

- Torres A, Vincent JA, Everett A, et al. Balloon valvuloplasty for congenital aortic stenosis: multi-center safety and efficacy outcome assessment. *Catheter Cardiovasc Interv* 2015; 86: 808-820.
- Sullivan PM, Rubio AE, Johnston TA, Jones TK. Long-term outcomes and re-interventions following balloon aortic valvuloplasty in pediatric patients with congenital aortic stenosis: a single-center study. *Catheter Cardiovasc Interv* 2017; 89: 288-296.
- Soulatges C, Momeni M, Zarrouk N, et al. Long term results of balloon valvuloplasty as primary treatment for congenital aortic valve stenosis: a 20-year review. *Pediatr Cardiol* 2015; 36: 1145-1152.
- Zoghbi WA, Enriquez-Sarano M, Foster E, et al; American Society of Echocardiography. Recommendations for evaluation of the severity of native valvular regurgitation with two dimensional and Doppler echocardiography. *J Am Soc Echocardiogr* 2003; 16: 777-802.
- Michel PL, Vahanian A, Besnainou F, Acar J. Value of qualitative angiographic grading in aortic regurgitation. *Eur Heart J* 1987; 8: 11-14.
- Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease: technique, indications and interpretations in 700 cases. *Am J Cardiol* 1964; 14: 437-447.
- Stapleton GE. Transcatheter management of neonatal aortic stenosis. *Cardiol Young* 2014; 24: 1117-1120.
- Ewert P, Bertram H, Breuer J, et al. Balloon valvuloplasty in the treatment of congenital aortic valve stenosis-a retrospective multicenter survey of more than 1000 patients. *Int J Cardiol* 2011; 149: 182-185.
- Maskatia SA, Ing FF, Justino H, et al. Twenty-five year experience with balloon aortic valvuloplasty for congenital aortic stenosis. *Am J Cardiol* 2011; 108: 1024-1028.
- Lababidi Z, Wu JR, Walls JT. Percutaneous balloon aortic valvuloplasty: results in 23 patients. *Am J Cardiol* 1984; 53: 194-197.
- Maskatia SA, Justino H, Ing FF, Crystal MA, Mattamal RJ, Petit CJ. Aortic valve morphology is associated with outcomes following balloon valvuloplasty for congenital aortic stenosis. *Catheter Cardiovasc Interv* 2013; 81: 90-95.
- McCrinkle BW, Blackstone EH, Williams WG, et al; and the members of the Congenital Heart Surgeons Society. Are outcomes of surgical versus transcatheter balloon valvotomy equivalent in neonatal critical aortic stenosis? *Circulation* 2001; 104(12 Suppl 1): I152-I158.
- Zain Z, Zadinello M, Menahem S, Brizard C. Neonatal isolated critical aortic valve stenosis: balloon valvuloplasty or surgical valvotomy. *Heart Lung Circ* 2006; 15: 18-23.
- Akdeniz C, Erdem A, Demir F, et al. Our medium-term results with aortic balloon valvuloplasty and factors affecting development of aortic regurgitation. *Anadolu Kardiyoloji Dergisi* 2011; 11: 329-335.
- Tokel NK, Ekici E, Kutsal A, İkizler C. Konjenital aort darlıklarında balon valvüloplasti: Erken ve orta dönemli sonuçlar. *Türk Kardiyoloji Derneği Arşivi* 1997; 25: 108-113.
- Nişli K, Karaca S, Dindar A. Balloon valvuloplasty for aortic stenosis using umbilical vein access in a newborn: first experience in Turkey. *Turk Kardiyol Dern Ars* 2016; 44: 521-523.
- Reich O, Tax P, Marek J, et al. Long term results of percutaneous balloon valvoplasty of congenital aortic stenosis: independent predictors of outcome. *Heart* 2004; 90: 70-76.
- Balmer C, Beghetti M, Fasnacht M, Friedli B, Arbenz U. Balloon aortic valvoplasty in paediatric patients: progressive aortic regurgitation is common. *Heart* 2004; 90: 77-81.
- McElhinney DB, Lock JE, Keane JF, Moran AM, Colan SD. Left heart growth, function, and reintervention after balloon aortic valvuloplasty for neonatal aortic stenosis. *Circulation* 2005; 111: 451-458.
- Latiff HA, Sholler GF, Cooper S. Balloon dilatation of aortic stenosis in infants younger than 6 months of age: intermediate outcome. *Pediatr Cardiol* 2003; 24: 17-26.
- Hill GD, Ginde S, Rios R, Frommelt PC, Hill KD. Surgical valvotomy versus balloon valvuloplasty for congenital aortic valve stenosis: a systematic review and meta-analysis. *J Am Heart Assoc* 2016; 5: e003931.
- Crespo D, Miró J, Vobecky SJ, et al. Experience in a single centre with percutaneous aortic valvoplasty in children, including those with associated cardiovascular lesions. *Cardiol Young* 2009; 19: 372-382.

23. Brown DW, Dipilato AE, Chong EC, et al. Sudden unexpected death after balloon valvuloplasty for congenital aortic stenosis. *J Am Coll Cardiol* 2010; 56: 1939-1946.
24. Fratz S, Gildein HP, Balling G, et al. Aortic valvuloplasty in pediatric patients substantially postpones the need for aortic valve surgery: a single-center experience of 188 patients after up to 17.5 years of follow-up. *Circulation* 2008; 117: 1201-1206.
25. Hamidi-Manesh L, Tibby SM, Herman R, Rosenthal E, Qureshi SA, Krasemann T. Influence of balloon size on aortic regurgitation in neonates undergoing balloon aortic valvuloplasty-a retrospective study over an 11-year period. *J Interv Cardiol* 2013; 26: 200-207.
26. Lewin RF, Dorros G, King JF, Seifert PE, Schmahl TM, Auer JE. Aortic annular tear after valvuloplasty: the role of aortic annulus echocardiographic measurement. *Cathet Cardiovasc Diagn* 1989; 16: 123-129.
27. Tuo G, Khambadkone S, Tann O, et al. Obstructive left heart disease in neonates with a "borderline" left ventricle: diagnostic challenges to choosing the best outcome. *Pediatr Cardiol* 2013; 34: 1567-1576.
28. Lofland GK, McCrindle BW, Williams WG, et al. Critical aortic stenosis in the neonate: a multi-institutional study of management, outcomes, and risk factors. *J Thorac Cardiovasc Surg* 2001; 121: 10-27.
29. Han RK, Gurofsky RC, Lee KJ, et al. Outcome and growth potential of left heart structures after neonatal intervention for aortic valvestenosis. *J Am Coll Cardiol* 2007; 50: 2406-2414.
30. Rossi RI, Manica JL, Petraco R, Scott M, Piazza L, Machado PM. Balloon aortic valvuloplasty for congenital aortic stenosis using the femoral and the carotid artery approach: a 16-year experience from a single center. *Catheter Cardiovasc Interv* 2011; 78: 84-90.
31. Brown DW, Dipilato AE, Chong EC, Lock JE, McElhinney DB. Aortic valve reinterventions after balloon aortic valvuloplasty for congenital aortic stenosis intermediate and late follow-up. *J Am Coll Cardiol* 2010; 56: 1740-1749.
32. d'Udekem Y, Siddiqui J, Cameron CS, et al. Long-term results of a strategy of aortic valve repair in the pediatric population. *J Thorac Cardiovasc Surg* 2013; 145: 461-469.
33. Petit CJ, Maskatia SA, Justino H, Mattamal RJ, Crystal MA, Ing FF. Repeat balloon aortic valvuloplasty effectively delays surgical intervention in children with recurrent aortic stenosis. *Catheter Cardiovasc Interv* 2013; 82: 549-555.
34. Miyamoto T, Sinzobahamvya N, Wetter J, et al. Twenty years experience of surgical aortic valvotomy for critical aortic stenosis in early infancy. *Eur J Cardiothorac Surg* 2006; 30: 35-40.
35. Friedman KG, Schidlow D, Freud L, Escobar-Diaz M, Tworetzky W. Left ventricular diastolic function and characteristics in fetal aortic stenosis. *Am J Cardiol* 2014; 114: 122-127.
36. Han RK, Gurofsky RC, Lee KJ, et al. Outcome and growth potential of left heart structures after neonatal intervention for aortic valve stenosis. *J Am Coll Cardiol* 2007; 50: 2406-2414.
37. Podnar T, Berden P, Vesel S. Balloon dilation of neonatal critical aortic valvar stenosis via the umbilical artery. *Cardiol Young* 2009; 19: 278-281.
38. Kim DW, Raviele AA, Vincent RN. Use of a 3 French system for balloon aortic valvuloplasty in infants. *Catheter Cardiovasc Interv* 2005; 66: 254-257.
39. Moore P, Egito E, Mowrey H, Perry SB, Lock JE, Keane JF. Midterm results of balloon dilation of congenital aortic stenosis: predictors of success. *J Am Coll Cardiol* 1996; 27: 1257-1263.