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Percutaneous Balloon Valvuloplasty for the Treatment of Isolated Pulmonary Valve Stenosis in Infants - A Single Centre Experience

ABSTRACT

Objectives: Pulmonary stenosis (PS) is a common congenital heart defect characterized by obstruction from the right ventricle to the pulmonary arteries. Few studies evaluate the long-term outcomes of the procedure, especially the degree of pulmonary regurgitation. We assessed the outcomes of infants following valvuloplasty for pulmonary valve stenosis.

Methods: We conducted a retrospective analysis of children with pulmonary valve stenosis who underwent pulmonary balloon valvuloplasty (BPV) at a single institution. Clinical summaries, catheterization data, and echocardiographic data were reviewed. The inclusion criteria were isolated balloon pulmonary valvuloplasty for pulmonary valve stenosis, with age <2 months at the time of intervention.

Results: Between 2006 and 2019, 104 patients underwent BPV for isolated PS. A total of 78 patients met the inclusion criteria. The median age at valvuloplasty was 6.5 days (1-60 days). The median last follow-up after valvuloplasty was 23.5±33.6 months. Pre-operative peak instantaneous pulmonary gradient (PIPG) measured by echocardiography was 70 (35-120) mmHg, which reduced to 26 (10-70) mmHg post-procedure. At the last follow-up, the gradient was 25 (0-100) mmHg. The mean balloon/annulus ratio was 1.18±0.12. Concerning the development of pulmonary regurgitation, mild pulmonary regurgitation was most observed [in 36 patients (46%)], and no patient developed severe regurgitation. Additionally, a correlation was found between female gender, preoperative gradient, pulmonary valve structure, and high residual gradient (p<0.0001, R>700).

Conclusion: Pulmonary balloon valvuloplasty remains a safe and effective treatment for children with isolated pulmonary valve stenosis, with excellent long-term outcomes and no mortality. Although the rate of reintervention is high in cases with a low mean balloon/annulus diameter ratio, the rate of pulmonary regurgitation is significantly lower.

Keywords: Balloon pulmonary valvuloplasty, infants, pulmonary stenosis, pulmonary regurgitation

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Pulmonary valve stenosis (PS) is one of the most common forms of Congenital Heart Diseases (CHD), occurring in approximately 0.7/1000 live births (1). Historically, surgical pulmonary valvotomy and valvectomy were the main treatments for relieving severe PS (2-4). However, in modern times, pulmonary balloon valvuloplasty has become the treatment of choice for children with moderate, severe, and critical pulmonary valve stenosis. It is widely considered a safe and effective treatment (5). Following the initial description of percutaneous balloon pulmonary valvuloplasty (BPV) by Kan and colleagues in 1982, this non-surgical technique emerged as the preferred initial treatment for moderate, severe, and critical PS (6). Generally, it is recommended that the procedure be performed when peak-to-peak gradients exceed 50 mmHg. The technique involves positioning one or more balloon catheters across the stenotic valve, usually over an extra-stiff guide wire, and inflating the balloons with diluted contrast material to produce valvotomy (7).

Although BPV can effectively relieve PS, long-term outcomes following BPV are not well documented in extensive cohorts. Only a few studies have evaluated the long-term results after pulmonary balloon valvuloplasty for pulmonary valve stenosis, especially concerning the incidence of pulmonary regurgitation. Instances of pulmonary valve replacement due to symptomatic right ventricular (RV) volume overload and PR following BPV have also been documented (8). This study aims to assess long-term outcomes in children younger

than 2 months who underwent pulmonary balloon valvuloplasty for isolated pulmonary valve stenosis at a single center.

METHODS

Ethics committee approval was obtained from Sami Ulus Children's Hospital on 26.08.2021, under document number 2021/8-6. The study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its subsequent amendments.

We performed a retrospective analysis at our institution to evaluate the outcomes of pulmonary balloon valvuloplasty in infants with isolated pulmonary valve stenosis. The cardiac catheterization database was searched for all patients who underwent this procedure between 2006 and 2019. Inclusion criteria were as follows: age younger than 2 months and isolated pulmonary valve stenosis treated with pulmonary balloon valvuloplasty. Patients were excluded if they had supravalvular or subvalvular stenosis, or if they were older than 2 months at the time of the procedure.

Clinical reports, echocardiograms, and cardiac catheterization data were reviewed. Comparisons between pre- and post-catheterization data and echocardiographic data included: peak-to-peak pressure gradient across the pulmonary valve, pulmonary annulus diameter, pulmonary valve structure and right ventricular morphology, balloon size, and severity of pulmonary and tricuspid valve regurgitation (determined via echocardiography). Clinical data reviews focused on symptoms and signs, accompanying cardiac anomalies, prostaglandin usage, follow-up duration, and other interventions post-discharge.

Pulmonary balloon valvuloplasty was conducted using a standard technique. Angiographic images were obtained using a power injection cineangiogram of the right ventricle and right ventricular outflow tract. Initial right heart hemodynamic and oximetric data were collected. Appropriate balloon sizes for intervention were chosen, with diameters ranging between 110% and 140% of the pulmonary valve annulus diameter, as measured in both anteroposterior and left lateral views.

The primary outcome measure was the comparison of pulmonary valve peak instantaneous gradient using Doppler. Doppler echocardiography was performed prior to the pulmonary balloon valvuloplasty, post-procedure, and at the most recent follow-up. Peak-to-peak pressure gradients, as measured by cardiac catheterization across the pulmonary valve post-procedure, were extracted from the cardiac catheterization database. Outcomes related to pulmonary regurgitation, discharge timing, and follow-up duration were evaluated at the same time points.

Statistical Methods

A retrospective analysis was conducted to evaluate the outcomes of pulmonary balloon valvuloplasty in children with isolated pulmonary valve stenosis. The cardiac catheterization database was searched for patients aged less than 3 months who underwent pulmonary balloon valvuloplasty between January 2006 and July 2020.

The inclusion criteria were as follows: patients with isolated pulmonary valve stenosis who were younger than 2 months at the time of the procedure. Patients were excluded if they had other Congenital Heart Diseases (CHDs) affecting the right ventricular outflow.

Clinical reports, echocardiograms, and cardiac catheterization data were reviewed. Data comparisons between pre- and post-catheterization, as well as echocardiographic data, included: peak-to-peak pressure gradient across the pulmonary valve (as determined by catheterization), balloon size, pulmonary annulus size (measured both by echocardiography and catheterization), peak gradient, and severity of pulmonary regurgitation (determined via echocardiography).

Patients were categorized into the "Critical pulmonary stenosis" group if they met one or more of the following criteria:

- Ductus-dependent circulation
- Presence of suprasystemic right ventricular pressure
- Cyanosis
- Low cardiac output
- Multiorgan insufficiencies
- Metabolic acidosis when the duct is narrowed.

RESULTS

During the study period, 104 patients underwent pulmonary balloon valvuloplasty. Of these, 78 patients (42 male) met the inclusion criteria. The median age at the time of intervention was 6.5 days (range: 1-60 days), with 42 (53.8%) of them being between 0-7 days. The median body weight during the procedure was 3212 g (range: 1570-5000 g). The patients' demographic characteristics and pulmonary valve gradient are presented in Table 1.

Table 1. Patient Characteristics

Demographics	
Age at initial intervention (days)	6.5 (1-60)
Male sex n (%)	42 (53.8)
Weight at initial intervention (kg)	3.21 (1.5-5)
Critical PS n (%)	39 (50)
Baseline echocardiogram	
Pulmonary annulus diameter (mm) (std. deviation)	6.4 (±1.04)
RV-PA PIPG (mmHg)	70 (35-120)
Baseline catheterization data	
Pulmonary annulus diameter (mm) (std. deviation)	6.1 (±1.1)
Intervention data	
Balloon/annulus ratio (std deviation)	1.18 (±0.12)
Post-intervention data	
RV-PA PSEG (mmHg)	25 (4-86)
RV-PA PIPG (mmHg)	26 (10-70)
Last RV-PA PIPG (mmHg)	25 (0-100)
Pulmonary regurgitation	
None n (%)	26 (33)
Mild n (%)	36 (46)
Moderate n (%)	16 (21)
Severe	0

PS: Pulmonary stenosis, RV-PA PSAG: Right ventricle-pulmonary artery peak systolic ejection gradient, RV-PA PIPG: Right ventricle-pulmonary artery peak instantaneous pulmonary gradient.

Regarding symptoms, the majority of patients, 54 (69%), presented with a murmur. Physical examination revealed that the largest group was asymptomatic, comprising 45 (57.7%) patients.

In terms of valve structure:

- 34 patients (43.6%) had a narrow valve.
- 29 patients (37.2%) had a dysplastic valve.
- 15 patients (19.2%) had a valve structure near to pulmonary atresia.

The average pulmonary annulus diameter measured by catheterisation was 6.1 mm (±1.1). Balloon sizes used ranged from 4 mm x 2 cm to 10 mm x 2 cm, with 7 mm x 2 cm and 8 mm x 2 cm Tyshak II being the most commonly used sizes, employed in 42 patients (53.8%). The mean balloon/annulus ratio stood at 1.186±0.12.

The median pre-intervention right ventricle-pulmonary artery peak instantaneous pressure gradient, as measured by echocardiography, was 70 mmHg (range=35-120 mmHg). Post-intervention, the median peak systolic ejection gradient (PSEG) measured by catheterisation and the peak instantaneous pressure gradient via echocardiography were 25 mmHg (range=4-86 mmHg) and 26 mmHg (range=10-70 mmHg), respectively. The catheter and echocardiography results did not show significant differences (p>0.05). However, a significant difference was noted between right ventricular-pulmonary artery gradients before and after the intervention (p<0.001).

Analysis of tricuspid valve regurgitation revealed a significant decrease in its number and severity post-intervention (p<0.001). Before the procedure, 34 (43.5%) patients exhibited moderate to severe tricuspid regurgitation. This number declined to 22 (28.2%) post-procedure.

Of all patients, 39 (50%) were diagnosed with critical pulmonary stenosis. Descriptive summaries of pulmonary valve pressure gradients, based on echocardiography and cardiac catheterization for all time points, as well as other features of patients classified under critical pulmonary stenosis and non-critical pulmonary stenosis, are available in Table 2. Pre-intervention right ventricle-pulmonary artery peak instantaneous pressure gradients measured via echocardiography were 84 mmHg (range=44-120 mmHg) for critical PS patients and 65 mmHg (range=35-116 mmHg) for valvular PS patients. A significant difference in right ventricular-pulmonary artery gradients was noted when comparing critical and non-critical PS patients before the procedure (p<0.05). However, post-balloon pulmonary valvuloplasty gradients showed no significant disparity (p=0.35). Patients with critical PS were discharged later than those without. Subsequent echocardiographic evaluations revealed that patients who underwent balloon valvuloplasty due to critical pulmonary stenosis had a higher pulmonary gradient.

Before the intervention, 25 (64.1%) patients with critical pulmonary stenosis and 9 (23%) without had moderate-to-severe tricuspid regurgitation (p<0.01). Following balloon pulmonary valvuloplasty, these numbers dropped to 21 (53.8%) and 5 (10.3%) for patients with and without critical pulmonary stenosis, respectively.

Follow-Up

Among the 78 patients included in the study, the mean follow-up time was 23.5±33.6 months. There were no mortality cases during this period. Out of these 78 patients, 19 (48.7%) with critical PS required reintervention, while balloon pulmonary valvuloplasty was repeated in five (13.5%) patients with non-critical PS (see Table 3). The likelihood of needing reintervention was significantly higher among patients with critical PS (p=0.01).

In terms of pulmonary regurgitation development, mild pulmonary regurgitation was the most common, occurring in 35 patients (44.9%). Importantly, no patient developed severe regurgitation. When comparing the critical and non-critical PS groups, there was no significant difference regarding the degree of pulmonary regurgitation (p=0.36).

Table 2. Descriptive Summaries of Patients and Pulmonary Valve Pressure Gradients by Echocardiography and Cardiac Catheterisation

	Critical Pulmonary Stenosis						
	Positive			Negative			P
	Median	Min	Max	Median	Min	Max	
Age at initial intervention (day)	4	1	59	10	1	60	0.054
Weight at initial intervention (g)	3200	1570	5000	3300	2190	5000	0.95
Pulmonary annulus diameter (catheter)	5.4	3.8	8.3	6.7	4.9	8.4	**0.001**
Pulmonary annulus diameter (Echocardiography)	6	4	8	6.7	4.6	8.6	0.101
Balloon size	6x2	4x2	10x2	8x2	6x2	10x2	**0.001**
Balloon/Anulus ratio	1.18	0.89	1.58	1.18	0.86	1.43	0.83
Pre intervention RV-PA PIPG (mmHg)	84	44	120	65	35	116	**0.002**
Post intervention RV-PA PSEG (mmHg)	26.5	3	86	23	6	74	0.35
Post intervention RV-PA PIPG (mmHg)	30	10	70	25	10	60	0.36
Discharge time (days)	7	2	55	4	1	38	**0.002**
Follow-up time without intervention (month)	9	1	116	4	1	137	0.96
Last RV-PA PIPG (mmHg) with ECHO	35	2	100	20	0	94	**0.003**

PS: Pulmonary stenosis, RV-PA PSAG: Right ventricle-pulmonary artery peak systolic ejection gradient, RV-PA PIPG: Right ventricle-pulmonary artery peak instantaneous pulmonary gradient.

Table 3. Follow-up Data in Patients with Critical and Noncritical Pulmonary Stenosis

		Critical Pulmonary Stenosis				
		Positive		Negative		p
		n	%	n	%	
Degree of tricuspid regurgitation before intervention	None	9	23.1	19	48.7	**0.001**
	1	5	12.8	11	28.2	
	2	6	15.4	7	17.9	
	3	14	35.9	2	5.1	
	4	5	12.8	0	0.0	
Ductus existance before intervention	Yes	33	84.6	12	30.8	**0.010**
	No	6	15.4	27	69.2	
Prostoglandine usage	Yes	29	74.4	5	13.2	**0.001**
	No	10	25.6	33	86.8	
Degree of tricuspid regurgitation after intervention	None	10	25.6	24	61.5	**0.020**
	1	8	20.5	11	28.2	
	2	10	25.6	2	5.1	
	3	9	23.1	1	2.6	
	4	2	5.1	1	2.6	
Ductal stent implantation	Done	3	7.7	0	0.0	0.071
	None	36	92.3	39	100.0	
BT Shunt	Done	2	5.1	0	0.0	0.350
	None	37	94.9	39	100.0	
Degree of pulmonary regurgitation	None	11	28.9	15	38.5	0.360
	1	18	47.4	17	43.6	
	2	9	23.7	7	17.9	
Total number of repeated Balloon Pulmonary Valvuloplasty	None	20	51.3	32	86.5	**0.001**
	1	12	30.8	4	10.8	
	2	6	15.4	1	2.7	
	3	1	2.6	0	0.0	

BT: Blalock Taussig shunt.

Throughout the follow-up period, three (7.7%) patients with critical PS underwent ductal stent implantation due to low saturation and low cardiac output syndrome. Additionally, two (5.1%) patients with critical PS had a Blalock–Taussig (BT) shunt operation. On the other hand, patients with non-critical PS did not require any surgeries other than BPV.

The right ventricular-pulmonary artery gradient exceeded 50 in nine patients as measured in the catheter room post-intervention and in eight patients as measured by echocardiography. For three of these patients, both measurement methods showed a gradient exceeding 50. Delving into the specific characteristics of these patients:

- The first had a Dysplastic Valve combined with Severe Infundibular Stenosis.
- The second exhibited a Dysplastic Valve with a Balloon/annulus ratio of 0.8.
- The third presented with Infundibular Stenosis and Supravalvar Stenosis.

A correlation was identified between female gender, preoperative gradient, pulmonary valve structure, and a high residual gradient ($p<0.0001$, $R>700$).

DISCUSSION

In patients with isolated pulmonary valve stenosis, there is a rapid improvement in the pulmonary valve gradient following balloon pulmonary valvuloplasty. Consistent with the literature, our study found that the pulmonary gradient significantly decreased post-balloon pulmonary valvuloplasty in both critical and non-critical PS patients (3, 4). However, when assessing the long-term follow-up, the reintervention rate for patients with critical PS was higher in this study compared to other findings in the literature. In a recent study by Parent et al., (9) involving 53 patients with isolated pulmonary stenosis, the reintervention rate was reported to be a mere 6%. Devanagondi et al.'s (10) research on 103 patients with isolated pulmonary stenosis who underwent BPV indicated that only 7 patients (7%) needed reintervention. Conversely, in our study, 48.8% of patients with critical PS, 13.5% of those with non-

critical PS, and 31.6% of all patients necessitated at least one reintervention.

Distinct from the prevailing literature, our observation regarding the progression of pulmonary regurgitation revealed that the most severe pulmonary regurgitation in all our study's patient groups was of the second degree. This variance is believed to be related to the balloon/annulus diameter ratio. Past research has emphasized that the pulmonary valve can be effectively and safely dilated if the balloon diameter lies between 120% and 140% of the pulmonary annulus diameter. This particular range has proven to optimize the reduction of the valvar gradient without causing significant pulmonary regurgitation or other procedural complications (5, 11). In our study, the mean balloon/annulus diameter ratio was 1.18±0.12. Thus, it appears that our study recorded a lower rate of pulmonary regurgitation and a higher need for repeated balloon pulmonary valvuloplasty due to this diminished ratio. Devanagondi et al. documented that 60% of their patients experienced moderate to severe pulmonary regurgitation during extended follow-ups, with their study's median value for the balloon/annulus diameter ratio reported at 1.27 (10).

Merino-Ingelmo et al.'s (12) study covered a cohort of 48 patients over an extended follow-up period (ranging from 10–24 years). Within this study, PR was prevalent: 58.4% of patients displayed grade II PR, and 31.2% had grade III PR. Moreover, they demonstrated that PR escalated with time. However, in our research, when evaluating the most recent echocardiographies during extended follow-ups, no progression in the degree of pulmonary regurgitation was observed.

Study Limitations

This study has several limitations. One primary constraint is its retrospective design. Another limitation is the small sample size, attributable to the inclusion criteria of patients aged under two months and the exclusion of patients who did not consistently attend their follow-up appointments.

CONCLUSION

Pulmonary balloon valvuloplasty remains a reliable and effective treatment for children diagnosed with isolated pulmonary valve stenosis. The procedure boasts remarkable long-term results and zero mortality rate. Notably, while there is a heightened reintervention rate in cases exhibiting a diminished mean balloon/annulus diameter ratio, pulmonary regurgitation is observed less frequently. Over an average follow-up period of 23.5±33.6 months, this research illustrates the persistence of a low pulmonary transvalvular peak gradient and a reduced occurrence of moderate-to-severe pulmonary valve regurgitation.

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