Original Article

Immediate Therapeutic Outcomes and Medium-term Follow-up of Percutaneous Balloon Pulmonary Valvuloplasty in Infants with Pulmonary Valve Stenosis: A Single-center Retrospective Study

Dian Hong[1,2], Ming-Yang Qian[1], Zhi-Wei Zhang[1], Shu-Shui Wang[1], Jun-Jie Li[1], Yi-Fan Li[1], Tian Liu[1]

[1]Department of Pediatric Cardiology, Guangdong Cardiovascular Institute, Guangdong General Hospital, Guangdong Academy of Medical Science, Guangzhou, Guangdong 510100, China

[2]Shantou University Medical College, Shantou, Guangdong 515041, China

Abstract

Background: Percutaneous balloon pulmonary valvuloplasty (PBPV) is the preferred therapy for pulmonary valve stenosis (PVS). This study retrospectively reviewed recent PBPV outcomes in infants with PVS. The aim of this study was to evaluate factors associated with immediate therapeutic outcomes and restenosis during medium-term follow-up.

Methods: The study included 158 infants with PVS who underwent PBPV from January 2009 to July 2015. Demographic characteristics and patient records were reviewed, including detailed hospitalization parameters, hemodynamic data before and immediately after balloon dilation, cineangiograms, and echocardiograms before PBPV and at each follow-up. All procedures were performed by more than two experienced operators.

Results: Immediately after balloon dilation, the pressure gradient across the pulmonary valve decreased from 73.09 ± 21.89 mmHg (range: 43–151 mmHg) to 24.49 ± 17.00 mmHg (range: 3–92 mmHg; $P < 0.001$) and the right ventricular systolic pressure decreased from 95.34 ± 23.44 mmHg (range: 60–174 mmHg) to 52.07 ± 18.89 mmHg (range: 22–134 mmHg; $P < 0.001$). Residual transvalvular pressure gradients of 67.31 ± 15.19 mmHg (range: 50–92 mmHg) were found in 8.2% of patients, indicating poor therapeutic effects; 6.4% of patients had variable-staged restenosis at follow-up and 3.8% underwent reintervention by balloon dilation or surgical repairs. Further analysis demonstrated that the balloon/annulus ratio showed statistically significant differences ($P < 0.05$) among groups with different therapeutic effects and between the restenosis and no-stenosis groups. Binary logistic regression analysis further revealed that higher balloon/annulus ratio (odds ratio: 0.005, 95% confidence interval: 0–0.39) was an independent protective factor for restenosis. The rate of severe complications was 1.9%.

Conclusions: PBPV is a definitive therapy for infants with PVS based on its effectiveness, feasibility, and safety. Restenosis upon medium-term follow-up is relatively rare.

Key words: Balloon Valvuloplasty; Cardiac Catheterization; Infants; Pulmonary Valve Stenosis

Introduction

Pulmonary valve stenosis (PVS) is a common congenital heart defect that accounts for approximately 8–10% of cardiac birth defects.[1-3] Valvular PVS is the most common form of PVS and could be isolated or associated with other cardiac anomalies. Percutaneous balloon pulmonary valvuloplasty (PBPV) was first described by Kan *et al.* in 1982.[4] Since then, it has been improved to the point that it is now established as the preferred therapy for valvular PVS because of its safety and effectiveness. Due to improvements in diagnostic methods for infants, neonates, and fetuses, there are more valvular PVS cases requiring intervention in these early stages, especially for critical PVS. Previous

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Address for correspondence: Dr. Ming-Yang Qian, Department of Pediatric Cardiology, Guangdong Cardiovascular Institute, Guangdong General Hospital, Guangdong Academy of Medical Science, Guangzhou, Guangdong 510100, China
E-Mail: Qmy_gz17@163.com

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studies have mainly focused on procedural outcomes in older children and adults, while few have investigated a large population of infants. Thus, we retrospectively analyzed 158 cases of valvular PVS in infants who received PBPV in our pediatric cardiology department. The purpose was to evaluate factors associated with immediate therapeutic outcomes and restenosis during medium-term follow-up.

Methods

Ethical approval

The study protocol was approved by the Ethics Committee of Guangdong General Hospital. Informed consent was obtained from parents.

Study population and basic characteristics

We conducted a retrospective review of 158 cases of infant PVS in which PBPV was performed at the Pediatric Cardiology Department, Guangdong Cardiovascular Institute (Guangdong General Hospital), from January 2009 to July 2015. Infants with residual stenosis after previous surgical procedures were excluded. Patients with PVS accompanied by patent foramen ovale, patent ductus arteriosus, atrial septal defects (ASDs), or ventricular septal defects (VSDs) without hemodynamic compromise were included. All patients completed routine examinations before the procedure, which included complete blood counts, biochemistry, coagulation time, hepatic and renal function, arterial blood gas, 12-lead electrocardiography (ECG), chest radiography, and transthoracic echocardiography (TTE). Basic clinical data were recorded, including demographics, date of birth, clinical manifestations, systemic arterial oxygen saturation (SaO_2), ECG results, date of procedure, height, and weight. TTE was carried out using an IE33 (Philips, Bothell, WA, USA) and a Vivid 7 (GE Healthcare, Horten, Norway). Data included transvalvular pressure gradient, cardiac chamber size, and morphology of the right ventricle (RV) and pulmonary valve (PV).

All cases underwent TTE <3 months before hospitalization, and the results were considered mild when the peak gradient across the valve was <36 mmHg, moderate for 36–64 mmHg, and severe when >64 mmHg. Although Doppler gradient may be overestimated, it was used as a noninvasive screening if clinically suspected.[5] Cardiac catheterization was recommended for PVS with transvalvular pressure gradients >36 mmHg, which was calculated by the Bernoulli equation using peak velocities obtained by continuous-wave Doppler echocardiographic measurements.[6] Finally, periprocedural complications were documented.

Procedural technique and data

All procedures were performed by two or more operators under general anesthesia. Neonates or infants with critical PVS had mechanical ventilation for respiratory support. Heart rate, respiration, ECG, and pulse oximetry were continuously monitored throughout the procedures. In high-risk cases, arterial lines were established for arterial blood pressure monitoring. The entry site was the femoral vein.

Hemodynamic assessment and biplane RV angiography (anterior-posterior views and lateral views) were performed for analyses before balloon pulmonary valvuloplasty (BPV). Iodixanol injection (Visipaque) (GE Healthcare) was used as a contrast medium. In this study, PVS severity grading was determined by the systolic pressure gradient across the PV (measured by catheterization), which has some differences from echocardiography.[5] According to hemodynamic assessments, PVS severity was considered mild when the pressure gradient was <40 mmHg, moderate when ranging from 40 to 60 mmHg, and severe when >60 mmHg.[7] Morphological assessments including the size of the pulmonary annulus and orifice were recorded. The size of the valve annulus was measured from a frame of the lateral projection of the cineangiogram and corrected for magnification. The size of inflated balloons (Balt, France) was selected according to the pulmonary annulus diameter; balloon diameters were 1.2–1.4 times the annulus diameter.[1] In some critical PVS cases with pinhole orifices, we used a coronary balloon (Cordis, FL, USA) for staged dilation. Balloons were inflated with diluted contrast material (1:4) several times until the waist disappeared.

Hemodynamic measurements and angiography were repeated to assess immediate therapeutic outcomes. According to the pressure gradient across the PV, measured immediately after balloon dilation, patients of different therapeutic effects were divided into three groups: pressure gradient ≤25 mmHg was the optimal effect (Group A), 25–50 mmHg was the suboptimal effect (Group B), and ≥50 mmHg was the poor effect (Group C).[1] Successful cases were defined as those with optimal or suboptimal effects that showed a clear relief of RV obstruction. Demographic and hemodynamic parameters were then compared among groups.

Medium-term follow-up protocol

After BPV, TTE was performed during hospitalization to assess the pressure gradient, valve opening, pulmonary and tricuspid regurgitation, and other morphological changes. Follow-up TTE was performed at 1 and 6 months, and then every year. At each follow-up visit, restenosis was noted. Restenosis was defined as an increase in the pressure gradient to ≥50 mmHg after successful dilation.[2]

Statistical analysis

All tests were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). Measurement data were expressed as mean ± standard deviation (SD), with associated ranges. Variables were compared using a paired *t*-test (two groups) or analysis of variance (more than two groups). Categorical data were recorded as counts and percentages, and difference was tested using the Chi-square test. Logistic regression analysis was performed to identify independent risk factors for restenosis. The beta-coefficient (β), odds ratio (*OR*), and corresponding 95% confidential interval (*CI*) were calculated. The level of statistical significance was set at $P < 0.05$.

Results

Patient demographics and baseline characteristics

There were 165 infants diagnosed with congenital isolated PVS. Among them, seven cases had mild PVS according to hemodynamic assessments; these were left for follow-up. Ultimately, 158 infants (98 male and 60 female) received PBPV. Average age at the time of the procedure was 5.41 ± 3.36 months (range: 9 days to 12 months), and average weight was 6.89 ± 2.10 kg (range: 2.5–12 kg). Among the patients, 10 were neonates and more than half (60%) were <6 months old. There were 31 infants (20%) who weighed <5 kg and 142 (90%) <10 kg. Patients were presented because of cyanosis, shortness of breath, feeding problems, or heart murmurs. The SaO_2 ranged from 53% to 100%. There were 41 patients (26%) with significant cyanosis and SaO_2 <90%.

All diagnoses were confirmed by TTE, and 123 infants (78%) were classified as severe PVS with peak gradients across the valve of >64 mmHg.[5] The associated heart lesions included ASD or patent foramen ovale in 112 patients (71%), small patent ductus arteriosus in 25 patients (16%), and small VSD in four patients (3%). Those with intracardiac shunts did not show hemodynamic compromise. The average hospitalization time was 7.71 ± 5.80 days (range: 2–51 days). Twenty-nine infants (18%) in critical situations required mechanical ventilation during the procedures.

Hemodynamic assessment

Before BPV, right ventricular systolic pressures (RVSPs) were 95.34 ± 23.44 mmHg (range: 60–174 mmHg). The pressure gradient across PV was 73.09 ± 21.89 mmHg (range: 42–151 mmHg). Severe PVS was confirmed in 104 infants (66%). The average pulmonary annulus diameter was 9.85 ± 1.85 mm, as measured by angiography.

Balloon selection

The balloon/annulus ratio indicates the ratio of the balloon diameter to that of the pulmonary annulus. Balloon sizes listed by the manufacturer were used to calculate this ratio. The average balloon/annulus ratio was 1.34 ± 0.17. There were 36 infants (23%) who required coronary balloons for staged dilation.

Immediate therapeutic results

Immediately after BPV, the pressure gradient reduced significantly from 73.09 ± 21.89 mmHg (range: 42–151 mmHg) to 25.05 ± 17.07 mmHg (range: 3–92 mmHg; $P < 0.001$). RVSP decreased significantly from 95.34 ± 23.44 mmHg (range: 60–174 mmHg) to 52.07 ± 18.89 mmHg (range: 22–134 mmHg; $P < 0.001$). Group A comprised 101 infants (64%) for whom pressure gradient decreased to 14.64 ± 5.63 mmHg (range: 3–25 mmHg); in Group B, the pressure gradient decreased to 34.93 ± 6.17 mmHg (range: 26–47 mmHg) consisted of 44 infants (28%); and Group C comprised 13 infants (8.2%) for whom the residual pressure gradient was 67.31 ± 15.19 mmHg (range: 50–92 mmHg). Angiography after balloon valvuloplasty was used to assess the reasons for poor effects. Right ventricular reactive spasm was the most common reason, occurring in 11 infants (Patient Nos. 16, 25, 36, 55, 90, 112, 113, 114, 129, 133, and 139). This was followed by residual hypertrophic muscle bundle in one infant (Patient No. 146) and valve dysplasia in one infant (Patient No. 144).

Univariate analysis was carried out among the different groups. Variables included procedural age, weight, balloon/annulus ratio, RVSP (pre-BPV), pressure gradient (pre-BPV), and staged dilation. The results revealed that the RVSP (pre-BPV; $P < 0.001$), pressure gradient (pre-PBPV; $P < 0.001$), and balloon/annulus ratio ($P < 0.05$) showed statistically significant differences among the groups. Demographic and procedural data among the different therapeutic groups are compared in Table 1.

Follow-up and restenosis

Outpatient follow-ups were performed 1 and 6 months after the procedure, and then every year. Four patients were excluded during the follow-up. Patient No. 114 failed to follow-up after leaving the hospital. Patient No. 121 was a 4 kg, 1-month-old female who died of ventricular fibrillation 6 months after the procedure with suspicion of the right heart failure as enlargement of the right atrium (RA) and RV were detected by bedside TTE. Patient No. 138 was a 3.3 kg, 1-month-old female with a pressure gradient still at 82 mmHg 1 day after the procedure and severe cyanosis

Table 1: Demographic characteristics and procedural date of infants in different therapeutic groups immediately after PBPV

Variables	Optimal group (n = 101)	Suboptimal group (n = 44)	Poor group (n = 13)	F/χ^2	P
Age (days)	171.24 ± 101.22	152.00 ± 97.70	127.69 ± 107.36	1.394	0.251
SaO_2 (%)	90.98 ± 9.81	90.41 ± 9.81	90.54 ± 10.45	0.056	0.946
Weight (kg)	7.03 ± 2.15	6.68 ± 2.10	6.30 ± 1.77	0.905	0.407
BAR	1.34 ± 0.15	1.36 ± 0.23	1.22 ± 0.12*,†	3.472	0.033
Pre-BPV RVSP (mmHg)	88.11 ± 20.53	105.82 ± 22.02*	116.00 ± 26.07*	17.054	<0.001
Pre-BPV PG (mmHg)	65.72 ± 18.29	85.11 ± 22.29*	89.62 ± 21.41*	19.776	<0.001
Female, n	40	16	4	0.449	0.799
Staged dilation, n	23	11	2	0.527	0.768

Data are expressed as number or median ± SD. *Compared with optimal group, P<0.05; †Compared with suboptimal group, P<0.05. SaO_2: Arterial oxygen saturation; BAR: Balloon/annulus ratio; BPV: Balloon pulmonary valvuloplasty; RVSP: Right ventricular systolic pressure; PG: Pressure gradient; PBPV: Percutaneous balloon pulmonary valvuloplasty; SD: Standard deviation.

who was ultimately referred for surgical repair 5 days later. Patient No. 142 was a 3 kg, 2-month-old male with congenital rubella syndrome and had developed multiple organ anomalies; he died of circulatory failure during the procedure.

Variable-staged restenosis presented in 6.4% of cases (10 in 154). Patient Nos. 62, 72, and 150 received surgical repair 8, 2, and 5 months after PBPV, respectively. Patient Nos. 5, 137, and 157 underwent repeated PBPV at 1 year, 2 years, and 4 months, respectively. Patient Nos. 37, 96, and 141 had spontaneous restenosis release during follow-up, and Patient No. 82 was still in follow-up.

Univariate analysis was conducted between the restenosis and no-stenosis groups. Variables included procedural age, weight, balloon/annulus ratio, RVSP (pre- and post-BPV), pressure gradient (pre- and post-BPV), and staged dilation. These results demonstrated that the balloon/annulus ratio in the two groups had statistically significant differences ($P < 0.05$) [Table 2]. Binary logistic regression analysis further revealed that a higher balloon/annulus ratio (*OR*: 0.005, 95% *CI*: 0–0.39) was an independent protective factor for restenosis [Table 3].

Complications

Severe complications occurred in 1.9% of patients (Patient Nos. 79, 95, and 142) in this study. Guidewire perforation causing cardiac tamponade occurred in Patient No. 95. Emergent operative exploration found injury to the RA. Patient No. 79 had a rupture of the tricuspid chordae tendineae during the procedure causing severe tricuspid regurgitation, which was finally repaired through surgery. Patient No. 142 had multiple organ anomalies and died from circulatory failure during the procedure as mentioned before.

Vascular complications occurred in three cases. Patient No. 6 had an arteriovenous fistula that resolved spontaneously. Patient No. 74 was found pale and pulseless in the right lower limb after the procedure. A right femoral arterial occlusion of 5 mm was found by computed tomography angiography. Anticoagulation and thrombolytic therapies failed, and one week later, the patient was referred for embolectomy. Patient No. 121 had an occlusion of the external iliac artery, but the blood supply to the limb was not affected. Thus, she left hospital and was followed up. The patient died of ventricular fibrillation 6 months later as mentioned previously.

Patient No. 47 had atrial flutter during the procedure and electrical cardioversion was carried out. Other complications including transient bradycardia and a drop in systemic blood pressure were common, especially for critical cases.

Discussion

PVS accounts for 8–10% of all congenital heart defects,[1-3] occurring in approximately 6.6/1000 live births and slightly higher in Asian countries compared to Europe and the United States.[8,9] In the past, surgical repair was the only choice. Kan *et al.* first reported PBPV as a new method for treating PVS in 1982.[4] Tynan *et al.* then described the application of PBPV for a 6-day-old infant with PVS.[10] As catheterization techniques developed and spread, PBPV replaced surgical repair in most PVS cases.[3] We began performing PBPV at our center in 1984. Rao performed a detailed study of PVS,[2] and later thoroughly discussed the

Table 3: Logistic regression analysis of risk factors for restenosis after PBPV

Variables	β	*OR*	95% *CI*
Age	0.008	1.008	0.995–1.023
Gender	−0.456	0.634	0.161–2.49
Weight	−0.476	0.621	0.298–1.295
BAR	−5.366	0.005	0–0.39
Staged dilation	−1.316	0.268	0.046–1.557
Pre-BPV RVSP	−0.068	0.934	0.813–1.073
Pre-BPV PG	0.074	1.076	0.932–1.243
Post-BPV RVSP	0.015	1.015	0.923–1.116
Post-BPV PG	−0.004	0.996	0.899–1.103
Constant	7.851	2569.158	

β: Logistic correlation coefficient; *OR*: Odds ratio; *CI*: Confidence interval; BAR: Balloon/annulus ratio; BPV: Balloon pulmonary valvuloplasty; RVSP: Right ventricular systolic pressure; PG: Pressure gradient; PBPV: Percutaneous balloon pulmonary valvuloplasty.

Table 2: Demographic characteristics and procedural date of infants in no-stenosis and restenosis groups at medium-term follow-up

Variables	No stenosis ($n = 144$)	Restenosis ($n = 10$)	t/χ^2	*P*
Age (days)	166.10 ± 101.34	145.17 ± 94.85	0.690	0.491
SaO_2 (%)	91.47 ± 9.13	85.83 ± 13.82	1.388	0.191
Weight (kg)	7.02 ± 2.10	6.11 ± 1.57	1.451	0.149
BAR	1.35 ± 0.17	1.21 ± 0.17	2.776	0.006
Pre-BPV RVSP (mmHg)	95.06 ± 23.43	97.92 ± 27.34	0.401	0.689
Pre-BPV PG (mmHg)	72.70 ± 21.92	76.83 ± 24.91	0.621	0.535
Post-BPV RVSP (mmHg)	51.46 ± 19.28	56.25 ± 15.48	0.837	0.404
Post-BPV PG (mmHg)	24.57 ± 17.34	28.92 ± 14.66	0.842	0.401
Female, *n*	54	4	0.001	1.000
Staged dilation, *n*	29	3	0.397	0.529

Data are expressed as number or median ± SD. $P<0.05$. SaO_2: Arterial oxygen saturation; BAR: Balloon/annulus ratio; BPV: Balloon pulmonary valvuloplasty; RVSP: Right ventricular systolic pressure; PG: Pressure gradient; SD: Standard deviation.

techniques and refinements of this procedure with regard to avoiding complications.[11] Cuypers *et al.* recently reviewed updates in the diagnosis and management of PVS.[3] In China, an experts' consensus was published in 2011 by the Committee On Congenital Heart Diseases of Cardiovascular Diseases Branch in Chinese Physicians' Association.[1] Their guidelines are still applied in China. The consensus opinion mentions that the most appropriate age to perform PBPV is between 2 and 4 years. Infants with PVS, especially critical cases, are indicated for PBPV. However, the occurrence of complications is more common in infants and neonates;[1,12,13] thus, we focused on infants in this study.

The main findings of this study indicate that PBPV is effective in the short- and medium-term follow-up with regard to safety and feasibility, as demonstrated by the immediate success rate of 92% and occurrence of restenosis in only 6.4% of cases.

Immediate therapeutic outcomes

PBPV can achieve satisfactory outcomes by relieving obstruction. In our study, infants receiving optimal therapeutic effects obtained nearly complete treatment, although there were some residual pressure gradients causing heart murmurs. Even in the group with suboptimal effects, relieving the obstruction in RV forward flow alleviated the pressure-loaded RV. The majority of patients in suboptimal group spontaneously resolved during follow-up. Furthermore, the results showed that poor therapeutic effects were related to the severity of initial PVS. The reason for poor therapeutic effects was hypertrophy of the infundibulum in severe cases and intolerance to the excitation of the dilated balloon. It is easier to have infundibulum reactive spasms after balloon dilation, which causes a pressure gradient across the right ventricular outflow tract (RVOT). Silvilairat *et al.* concluded that in cases of severe obstruction, significant residual pressure gradients would persist at the infundibular level but some could resolve later due to regression of the infundibular hypertrophy.[14] The balloon/annulus ratio was another factor associated with immediate therapeutic effects as well as the occurrence of restenosis, which will be discussed in detail later. Neither procedural age nor weight had a relationship with therapeutic effects.[15]

Similar to the results of our study, previous studies have reported the immediate effectiveness and safety of PBPV for different age groups.[13,14,16-24] Merino-Ingelmo *et al.* conducted a study of 53 pediatric patients with a success rate of 73.58% in all cases and 55.55% in those aged ≤3 months.[22] Holzer *et al.* carried out a multicenter study including 211 patients of which 172 were <1 year of age;[19] 88% of these patients achieved a reduction in their systolic gradient to ≤25 mmHg. In multivariable analysis, it was demonstrated that moderate or severe valve thickening and the presence of the supravalvular stenosis were independent risk factors of procedural failure.

The occurrence of severe complications was low in our study. For infants receiving PBPV, complications related to procedural mechanical injuries are markedly higher compared to the elder group, including damage to myocardium, perforation of the cardiac chamber,[16] rupture of the chordae tendineae, and other mild complications such as vascular injuries. Echigo described that the reason for the higher rate of major complications in critical PVS was the fragility of the RV and patient characteristics.[13] Fedderly *et al.* carried out PBPV in 12 infants with critical PVS or pulmonary atresia with intact ventricular septum and reported two cases of guidewire perforation of the RVOT.[25] However, results are variable between centers. Holzer *et al.* reported that arrhythmia was the most common adverse event.[19]

In the study by Gournay *et al.,* 82 newborns with critical PVS had a success rate of 88%. They also reported two intraprocedural deaths. One was previously confirmed to have Noonan syndrome with cardiomyopathy while the other died of myocardial dissection during angiography.[18] Other nonfatal but significant complications included balloon bursting, necrotizing enterocolitis, septic shock, abrupt closure of the ductus arteriosus, and cerebral thrombosis.[14,18] In our opinion, a well-equipped laboratory, with trained and cooperating operators experienced in the techniques, and multidisciplinary collaboration are essential to reduce the potential hazards.

Restenosis in medium-term follow-up

The rate of restenosis was 6.4% (10 of 158) in our study, and the rate of reintervention was 3.7% (6 of 158). Three restenosis patients had obstructions that spontaneously resolved later. The main reason was the development of valve annulus as the patients grew. Thus, valvular openings will gradually accommodate to the previously obstructed blood flow. Among the restenosis infants, reintervention procedures were selectable. For those with isolated dome-shaped PVS,[26] PBPV is recommended, as it is safe and minimally invasive. However, for those with dysplastic valves, supravalvular or infundibular stenosis, or accompanied by significant cardiac anomalies, it is better to choose surgical repair.

Further studies revealed that the balloon/annulus ratio was significantly associated with a higher ratio of preventing restenosis. Residual stenosis after successful dilation was unrelated to the severity of the original stenosis or the immediate outcomes of previous dilation. Some studies have stated that younger patients have a tendency to develop restenosis due to the poor growth capacity of the valve.[27] The results of our study showed that neither interventional age nor weight played roles in the occurrence of residual stenosis; Santoro *et al.* found similar results in their study.[24]

Balloon selection

With regard to balloon selection, both the immediate therapeutic effects and medium-term results were related to the balloon/annulus ratio according to our studies. To ensure the success of PBPV, it is crucial to select appropriate

balloons. Several previous studies have focused on the relationship between balloon selection and valve annulus; however, different conclusions were drawn. The most widely accepted ratio is 1.2–1.4, which has already been mentioned in some guidelines and recommendations.[1,2] We use this ratio in our clinical practice as well.

According to an early study by Rao, balloon/annulus ratios of 1.21–1.4 and >1.41 had similar intermediate-term results. It is clear that residual obstructions exist if balloons are <1.2 times the diameter of the annulus, while it would damage the RVOT without any change in therapeutic effects if the balloon diameter is >1.5 times the annulus. Rao believed that balloons 1.2–1.5 times the annulus diameter are the best option.[11] Later, McCrindle showed that the occurrence of pulmonary regurgitation increased with balloon/annulus ratios >1.4.[27]

We chose balloons that were 1.2–1.4 times the annulus and got a restenosis rate of 6.2%. Behjati-Ardakani *et al.* conducted a study in 98 patients of different age groups and used balloons 1.1–1.2 times the annulus diameter. The results demonstrated that the incidence of restenosis was 16.7% at 3 months and 11.4% at 1 year.[16] Silvilairat *et al.* investigated 25 patients using balloons 1.0–1.3 times the annulus diameter and the medium-term stenotic rate was 24% (six cases).[14] We preferred balloons that were at least 1.2–1.4 times the annulus. Our results show that it is preferable to use the largest balloon allowable given the patient's conditions. Balloons 1.4–1.5 times the annulus are recommended for PVS with dysplastic valve.[2]

However, balloon selection in the clinic requires comprehensive considerations. In infants with critical PVS, the pinhole orifice of the PV limits the use of relatively larger balloons; staged dilation is preferred. The goal is to widen the orifice of the valve to position the targeted-size balloon. Moreover, larger balloons have higher profiles. Thus, there is the potential to harm the assessed vessels and also an increased incidence of complications such as cardiac perforation. Future refinements in balloons and delivery sheaths are needed.

Procedural considerations for critical cases

With respect to periprocedural therapy and preparation for critical PVS, especially in neonates with severe cyanosis, we prefer to maintain continuous intravenous low-dose prostaglandin until after the procedure. Blood pressure monitoring is required at the same time. The purpose is to dilate the ductus arteriosus to increase pulmonary blood supply and increase oxygenation levels, with SaO_2 reaching at least 90%. Patients are likely to be maintained in stable condition before the procedure, minimizing the risk of emergencies.

The procedure should be performed with operating room and intensive care unit backup, and an ultrasonography machine should be on stand-by.

Manipulating the catheter into the RV is challenging because the RA is usually dilated with massive tricuspid regurgitation, while the RV cavity is shallow. A 5F Judkins right (JR) 3.5 diagnostic catheter (Cordis) advanced with a slippery 0.032" hydrophilic guidewire (Terumo, Japan) inside is helpful. Orient the catheter tip to the anterior–inferior direction to face the tricuspid valve, enabling easy passage into the RV. Advance the hydrophilic guidewire first if the catheter is hindered by the regurgitant flow. The whole process must be performed while continuously monitoring pressures through a transducer. Proceed until the appearance of tower waveforms, and then inject small doses of diluted contrast to ensure the correct RV position.

Rotate the catheter clockwise and gently pull to adjust the infundibulum construction. Selective angiography in RVOT is performed to mark the corrected location of the PV orifice. If it is well performed, there will be a clear view of the RVOT-PV in lateral projections.

A coronary balloon is first used for dilation when the orifice is smaller than 2 mm, as measured by angiogram. A balloon diameter of 4 mm is commonly used, while 5 mm is preferable to those with thick and adhesive leaflets.

A stiff exchange length guidewire (Cordis) is preferred to pass through the ductus arteriosus into the distal descending aorta. This provides a good support for balloon delivery and fixation. In addition, a stent could be implanted into the ductus arteriosus to ensure pulmonary circulation if the therapeutic effect is poor and there is no improvement in oxygenation after balloon dilation.

Percutaneous balloon pulmonary valvuloplasty and surgical repair

Studies found that fewer reinterventions for residual PVS are required after surgical repair compared with BPV. However, valve insufficiency is troublesome after surgery.[28] Roos-Hesselink *et al.* reported that pulmonary regurgitation was the most common reason for reoperation in surgical cases (nearly 9%) in a study with a more than 20-year follow-up period. Thus, the risk of RV dysfunction caused by massive regurgitation is probable in the future despite the advantage of a lower residual pressure gradient.[29] Reoperation will encounter more problems including tissue adhesion, while PBPV can be repeated several times in the same patient. PBPV is less invasive, less expensive, and requires shorter hospital stays.[28] Furthermore, there is less psychological discomfort and avoids an incision scar. Thus, PBPV remains the first choice therapeutic for isolated PVS.

However, in cases of PVS with dysplastic valve or RV hypoplasia, surgical repairs are recommended. The results of our study support this conclusion. In the study by Merino-Ingelmo *et al*., dysplastic valve morphology was another risk factor associated with success rate, which was only 25% compared with 73.58% among all patients.[22] Sehar *et al*. concluded that PBPV was suboptimal for dysplastic valve PVS.[30] PVS with valve dysplasia requires surgical valvotomy to reconstruct the valve and thoroughly relieve the obstruction. For PV cases accompanied with RV

hypoplasia, it is crucial to establish abundant forward flow to promote heart chamber development. Thus, only relieving the obstruction by PBPV is not sufficient. Moreover, RV hypoplasia leads to decreased RV compliance and persistent right to left shunts, even after the procedure. As described by Gournay *et al.*, RV compliance was an important factor affecting long-term success, and an effective way to overcome poor compliance was to place a surgical shunt.[18] Fedderly *et al.* studied 12 infants with critical PVS or pulmonary atresia with intact ventricular septum, and their results demonstrated that PBPV produced definitive therapeutic outcomes in infants who have tricuspid valve annulus >11 mm ($Z \geq -0.5$), PV annulus ≥7 mm ($Z \geq -1.5$) and RV volume >30 ml/m^2.[25] Finally, if the patient has accompanying ASD or VSD (hemodynamic compromise), it is better to choose radical repair procedures.

Due to the retrospective collection of clinical data, not all cases had complete datasets available, especially for procedural techniques. Moreover, we noticed that there was large variability in the echocardiography estimation of parameters. This depends on machine equipment, patient condition, and the experience of examiners.

This study does not include some parameters such as pulmonary regurgitation, tricuspid regurgitation, or cardiac function, which may be important for assessing reinterventions and complications during follow-up. Compared with residual stenosis, pulmonary regurgitation is prominent in patients undergoing surgical repairs.[29] Thus, we decided not to include it in our study. With regard to the tricuspid regurgitation, it was found in almost every case due to the augmented RV afterload. Tricuspid regurgitation will resolve following obstruction relief except in cases of accompanied right heart dysfunction. Cardiac function especially RV function plays a role in critical PVS. For the chronic increase in wall stress, it will result in concentric hypertrophy. Gradually, ventricular remodeling happens, finally causing ventricular dysfunction. In neonates and infants with critical PVS, the process happens in the fetus and directly interferes with RV development. In our study, all infants had TTE to identify PVS with RV hypoplasia, which is directly recommended for surgical repair. We believe that assessing right heart function in PVS could be a starting point for future studies.

In addition, this study only focused on acute and medium-term procedural outcomes. Long-term follow-up of procedural effectiveness is also of interest. The data in the study only applies to isolated PVS and is limited to patients with dysplastic valve or complex cardiac anomalies. Another limitation is that this study was performed at a single center. In the future, we hope to complete a multicenter study with larger sample sizes throughout China.

These results were derived from procedures documented over the past 8 years and represent recent cases at our center. PBPV is usually effective to relieve obstructions when successfully processed. Right ventricular reactive spasm was the most common reason for poor immediate therapeutic effects. In our experience, the rate of fatal complications and mortality were low, but highly qualified operators with skilled techniques and equipped laboratories are necessarily to ensure safety. Restenosis in medium-term follow-up was relatively rare (6.4%). Statistical analysis showed that relatively small balloon/annulus ratios accounted for the poor immediate effects and the occurrence of restenosis. Larger balloons in the acceptable range (1.2–1.4 times the annulus) are preferable. PBPV appears to sure palliation, but PVS with dysplastic valve or RV hypoplasias recommended to surgical repair. It is essential to thoroughly evaluate patient conditions to determine the best therapy.

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Conflicts of interest

There are no conflicts of interest.

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