ORIGINAL ARTICLE

Outcomes after Balloon Pulmonary Valvuloplasty for Critical Pulmonary Stenosis: A Tunisian reference center experience

Résultats de la Valvuloplastie Pulmonaire au Ballonnet pour Sténose Pulmonaire Critique : Expérience d'un centre de référence Tunisien

Ines Boudiche[1,3], Selim Boudiche[2,3], Rihab Ben Othmen[1,3], Hela Msaad[1,3], Abdeljalil Farhati[2], Kaouthar Hakim[1,3], Mohamed Sami Mourali[2,3], Fatma Ouarda[1,3]

1. Pediatric Cardiology Department, La Rabta Hospital, Tunis, Tunisia.
2. Cardiology Department, La Rabta Hospital, Tunis, Tunisia.
3. Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia.

Abstract

Introduction: Balloon pulmonary valvuloplasty (BPV) has emerged as the standard of care for critical pulmonary stenosis (CPS) in newborns. The aim of this study was to describe BVP results for CPS in a North African country where data are scarce.

Methods: A monocentric retrospective descriptive study was conducted on neonates who underwent BPV for CPS between 2000 and 2023, with a minimum clinical and echocardiographic follow-up of 12 months. Primary endpoint was immediate procedural success rate, and secondary endpoints were early additional procedures and late reinterventions.

Results: Thirty-four newborns were included. Median age was 10 days [4-17]. Gender-ratio was 1.4. Procedural success was observed in 73%. Six deaths (18%) were noted (two per-procedural and four during in-hospital phase). Early additional procedures were required in 16 patients (50%) consisting of prolonged prostaglandin-E1 infusion, three early BPV-redo and one early Blalock-Taussig shunt surgery. At 3-year median follow-up [1-5], six late reinterventions were reported in five patients (18%), for recurrent valvular or fixed subvalvular obstruction of the right ventricle (RV) outflow tract. These included four late BPV-redo and two late surgeries.

Incomplete results, bipartite RV and severe dynamic infundibular stenosis were associated with early additional procedures. The balloon-to-annulus ratio was significantly smaller in those requiring late reintervention (1.12±0.17 vs. 1.33±0.17, p=0.004).

Conclusion: BPV was an effective treatment for neonatal CPS, with an incompressible rate of additional early procedures related to incomplete results or bipartite RV, and late reinterventions often driven by recurrent valvular or fixed subvalvular obstruction of the RV outflow tract.

Keywords: Pulmonary valve stenosis, Critical, Newborn, Percutaneous balloon valvuloplasty, Outcomes.

Résumé

Introduction : La valvuloplastie percutanée au ballonnet (VPB) constitue le traitement de choix de la sténose pulmonaire critique (SPC) du nouveau-né. L'objectif de cette étude était de décrire les résultats de la VPB pour SPC dans un pays Nord-Africain.

Méthodes : Etude rétrospective incluant les nouveau-nés ayant bénéficié de VPB pour SPC entre 2000 et 2023, avec un suivi clinique et échocardiographique minimal de 12 mois. Le critère de jugement principal était le taux de succès procédural immédiat et les critères de jugement secondaires étaient la nécessité d'un geste additionnel précoce et de réinterventions tardives.

Résultats : Trente-quatre nouveau-nés inclus. Age médian 10 jours [4-17]. Genre-ratio 1,4. Le succès procédural immédiat était de 73%. Six décès (18%) ont été notés dont deux per-procéduraux et quatre à la phase hospitalière. Un geste additionnel précoce était nécessaire chez 16 patients (50%) s'agissant de perfusion de prostaglandines-E, trois re-VPB précoces et une chirurgie précoce. A trois ans [1-5], six réinterventions tardives ont été rapportées chez cinq patients (18%) pour une resténose valvulaire ou sous-valvulaire fixée de la voie d'éjection du ventricule droit s'agissant de quatre re-VPB et deux chirurgies tardives.

Un résultat incomplet, un ventricule droit bipartite et une sténose infundibulaire dynamique sévère étaient associés aux gestes additionnels précoces. Le ratio ballon-anneau pulmonaire était plus petit était associé aux réinterventions tardives (1,12±0,17 contre 1,33±0,17, p=0,004).

Conclusion : La VPB a constitué un traitement efficace de la SPC du nouveau-né, moyennant un taux incompressible de gestes additionnels précoces et de réinterventions tardives.

Mots clés : Sténose valvulaire pulmonaire, Critique, Nouveau-né, Valvuloplastie par ballonnet, Pronostic.

Correspondance

Ines Boudiche

Pediatric Cardiology Department, La Rabta Hospital, Tunis, Tunisia.

Email: inesboudiche@gmail.com

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Introduction

Critical pulmonary valve stenosis (CPS) is a rare but life-threatening congenital heart disease. It is characterized by a right ventricular outflow tract obstruction (RVOTO) with an intact interventricular septum, resulting in severely restricted pulmonary blood flow that is consequently dependent on ductus arteriosus (DA) patency (1–3).
Its manifestation often occurs early in the neonatal period, where newborns present with cyanosis with or without signs of right heart failure. Cyanosis is attributed to a right-to-left atrial shunt secondary to the right ventricle (RV) restrictive physiology (1,4–6). Prenatal diagnosis is also feasible (4).
Spontaneous course is fatal since CPS leads to RV failure and collapse constituting thus a diagnostic and therapeutic emergency, requiring rapid obstruction removal (4). In this setting, Doppler echocardiography is invaluable for diagnosing structural abnormalities, assessing hemodynamic consequences and planning urgent intervention (7).
In 1982, Kan et al (8,9) introduced the percutaneous technique of balloon pulmonary valvuloplasty (BPV) and this technique was subsequently applied to neonates with CPS. Currently, BPV is the treatment of choice for newborns with CPS (2,3,6,10–12). Surgery remains reserved for inaccessible and complex non-valvular forms (12).
Following BPV for CPS, patient prognosis varies significantly. Besides valvular involvement, CPS is associated with varying degrees of RV hypertrophy and hypoplasia, tricuspid valve and coronary circulation structural abnormalities, which will largely determine prognosis. The resulting RV dysfunction is more or less reversible after BPV. This may explain the need for early additional procedures and/or late reinterventions despite immediate procedural success (13).
Limited data are available on short and long-term outcomes of BPV for CPS (14–21). These were small sized sample series, evaluating heterogenous forms of pulmonary stenosis (PS) including pulmonary atresia with intact ventricular septum and severe PS besides CPS (10,22–25).
Aim of this study was to describe BPV results in the context of CPS within a North African reference center.

Methods

Study design

A monocentric retrospective descriptive study was conducted on neonates who underwent BPV for CPS over a 24-year period from January 2000 to December 2023 at a reference North African center, with a minimum clinical and echocardiographic follow-up of 12 months.

Study population

All neonates (infants under 28 days of age) who underwent BPV for CPS at the valvular level were included. CPS was strictly defined as a tight pulmonary valve stenosis present at birth with cyanosis and evidence of patent DA dependency (3). Patients with a diagnosis of SPS, pulmonary atresia with or without interventricular septal defect as well as patients with valvular PS and multiple levels of RVOTO were not included. Patients with complex congenital heart disease (heterotaxy syndromes, tricuspid atresia, Ebstein's disease, double outlet RV, transposition of great vessels and tetralogy of Fallot) in association with CPS were also not included. Patients whose records were incomplete or unusable, lost to follow-up immediately after BPV and whose parents did not consent to study participation were excluded.
Archives of the ultrasound laboratory and the catheterization rooms of Cardiology and Pediatric Cardiology Departments were consulted. Were collected 1) pre-procedural demographic, clinical, electrocardiographic and echocardiographic data 2) procedural angiographic and cardiac catheterization data, and 3) post-procedural intra-hospital and long-term follow-up data. Follow-up protocol was clinical and echocardiographic at 1, 3, 6, 12 months and then yearly.
Standardized echocardiographic views, along with color Doppler and continuous-wave assessments, were obtained for all patients. An independent pediatric echocardiography specialist reviewed and interpreted all images as part of routine clinical practice. Two-dimensional Doppler echocardiographic evaluations were conducted prior to and following BPV, as well as during each follow-up visit.
Each patient underwent BPV in the catheterization laboratory following a standardized protocol. Hemodynamic measurements, including right ventricular systolic pressure (RVSP), pulmonary artery systolic pressure, and right ventricular-to-pulmonary artery peak-gradient (PG) or transvalvular PG were recorded before and immediately after the procedure. Procedural details were documented, such as number, type, and size of balloons used, number of inflations for each balloon, maximum balloon-to-annulus ratio, presence of dynamic infundibular obstruction, and PG across RVOT.

Study endpoints

Primary endpoint was to describe immediate (procedural phase), short-term (in-hospital phase) and long-term results of BPV for CPS. To assess immediate results, procedural success rate and procedural complications were noted. Procedural success was defined as a post-BPV transvalvular PG < 25 mmHg or its reduction of at least 50% and a post-PVB SpO2 (Pulse Oxygen Saturation) > 85% (26,27). All complications up to patient death, such as respiratory or cardiac arrest, pericardial effusion, rhythm disorders or any vascular complication at the access site were recorded. To assess short-term results, the need for additional early procedures, as well as deaths in hospital were recorded. All additional early procedures performed including medical procedures such as prolonged Prostaglandins E1 (PGE1)-infusion and beta-blockers administration for dynamic infundibular stenosis or interventions to enhance pulmonary flow were noted, including early BPV-redo for incomplete results and DA stenting (28,29) or Blalock-Taussig shunt

(13,30) in cases of non-compliant RV. In the long term, beyond the hospital phase, were collected clinical and echocardiographic follow-up at 12 months and at the latest news, as well as late reinterventions: late BPV-redo or surgical valvulotomy in case of valvular restenosis (13), RV overhaul operation in case of fixed subvalvular stenosis (bi-ventricular repair) and Glenn operation period (1,5 ventricle repair) in case of non-compliant RV remaining after a 12-month expectant (13). Follow-up was updated to 31 December 2023. Secondary endpoint was to identify factors associated with post-procedural mortality, additional procedures use, and late reinterventions need.

Statistical analysis

All statistical analysis was performed using SPSS version 24.0. Continuous variables were expressed as mean ± standard deviation for parametric data, and median [interquartile range] for non-parametric data. Normality was determined using the Kolmogorov-Smirnov test. Qualitative variables were expressed as percentages. Comparisons were performed using non-parametric tests because of non-normally distributed data: Mann Whitney U, Pearson's chi-squared test and Fisher's exact test. A p-value <0.05 was considered statistically significant. Kaplan-Meier survival analysis curves were used to depict deaths and reinterventions during follow-up.

Results

A total of 64 newborns with PS were screened by consulting ultrasound laboratory and catheterization room archives during the study period. In accordance with the above-mentioned selection criteria, 34 newborns with CPS who had undergone BPV during the neonatal period were finally retained (Figure 1).

There was no family history of congenital heart disease. First-degree parents' consanguinity was noted in 3 cases (9%). Prenatal diagnosis was established in 4 cases (12%). Gender-ratio was 1.4. Median age at procedure was 10 days, with extremes ranging from 2 to 28 days. Initial examination revealed refractory cyanosis and pulmonary systolic murmur in all patients, tachypnea in 22 (65%) and right heart failure in one (3%). All patients were urgently put on PGE1 while awaiting BPV. Median SpO2 at baseline was 70% IQR [50-84%]. On PGE1, median SpO2 increased to 89% IQR [80-94%]. On electrocardiogram, sinus rhythm was noted in all cases except in one neonate who presented an atrial flutter with successful electrical cardioversion. A right axis and electrical RV hypertrophy were found in all neonates. Electrical right atrial hypertrophy was noted in 5 cases. All neonates had a prominent left middle arch on chest radiograph, indicative of post-stenotic dilatation of the pulmonary artery trunk, a right overhang indicative of dilatation of the right atrium, a convex right inferior arch indicative of RV hypertrophy and pulmonary hypovascularisation. Mean cardiothoracic index was 0.61 ± 0.06 (Table 1).

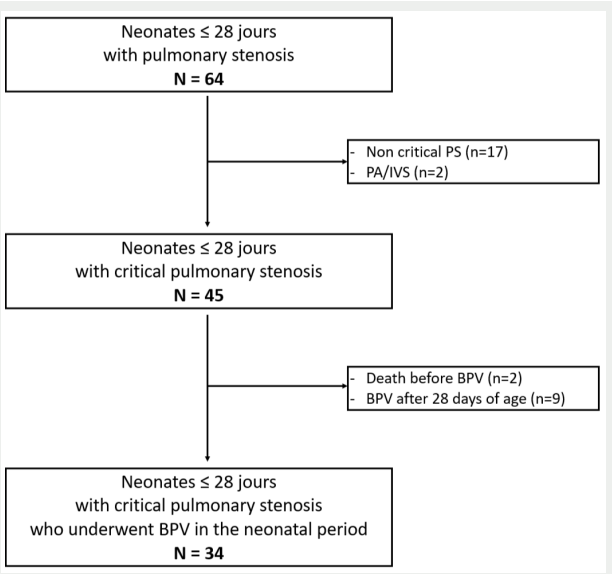

Figure 1. Study flow chart.

BPV: Balloon Pulmonary Valvuloplasty, **PA/IVS**: Pulmonary Atresia with Intact Ventricular Septum, **PS**: Pulmonary Stenosis.

Table 1. Baseline demographic and clinical characteristics of neonates with critical pulmonary stenosis.

Characteristics	Median (IQR) or Mean (σ) or Percentages; n=34
Demographic and clinical	
Males/Females	20/14
Age at procedure (days)	10 (4 – 17.2)
Height (cm)	49.7 ± 2.2
Weight (Kg)	3.15 ± 0.5
Term (WA)	39 (38 – 40)
Mother age (years)	32 (29 – 37.2)
Family history of CHD	0 (0%)
Consanguinity	3 (9%)
Prenatal diagnosis	4 (12%)
Cyanosis	34 (100%)
SpO2 pre PGE1 (%)	70 (50 – 84)
SpO2 post PGE1 (%)	89 (80 – 94)
Tachypnea	22 (65%)
Respiratory rate (cpm)	53 ± 13
Heart rate (bpm)	139 ± 18
RHF – Hepatomegaly	1 (3%)
Systolic BP (mmHg)	72 ± 8
Diastolic BP (mmHg)	39 ± 7
Mean BP (mmHg)	48 ± 6
Systolic murmur	34 (100%)
ECG	
Sinus rhythm / Atrial flutter	33/1
Right QRS axis	34 (100%)
RAH	5 (15%)
RVH	34 (100%)
Chest X-ray	
Cardiothoracic index	0.61 ± 0.06
Left middle arch salient	34 (100%)
Right overhang	34 (100%)
Convex lower right arch	34 (100%)
Pulmonary hypovascularisation	34 (100%)

BP: Blood Pressure, **CHD**: Congenital Heart Disease, **ECG**: Electrocardiogram, **PGE1**: Prostaglandins E1, **RAH**: Right Atrial Hypertrophy, **RHF**: Right Heart Failure, **RVH**: Right Ventricular Hypertrophy, **WA**: Weeks of amenorrhea.

Mean pulmonary annulus diameter was 6.4±0.9 mm with mean Z-score of -2.11±0.86. 59% of neonates had dysplastic PV. Mean transvalvular PG was 98±22 mmHg with extremes ranging from 62 to 140 mmHg. RV was bipartite in 5/34 patients (15%). Mean tricuspid annulus diameter was 11.7±3.2 mm with a mean Z-score of 0.90±2.92. Non-RV-dependent coronary artery fistulas were observed in 4/34 (12%) patients. Tricuspid regurgitation was present in all cases and was significant (grade≥3) in 19 cases (56%). RVSP averaged 108±23 mmHg, with extremes ranging from 60 to 155 mmHg.

BPV was performed under general anesthesia in all cases. Vascular access was via femoral vein in 33 patients (97%) and via umbilical vein in one patient (3%). Seventeen guidewires 0.014“, 14 guidewires 0.018” and 3 guidewires 0.025” were used to cross the PV. PV predilation was required in 10 cases (29%). BPV was performed using a dedicated balloon in 27 cases (79%) and coronary balloons in 6 cases (18%). Mean Balloon/Pulmonary-Annulus Ratio was 1.28 ± 0.18, with extremes ranging from 1 to 1.66.

Twenty-five immediate procedural successes (73%) were achieved. Seven incomplete results (21%) were noted, with significant residual valvular or dynamic sub-valvular stenosis, in 5 and 2 patients respectively. Two per-procedural deaths (6%) were recorded. The first followed extreme bradycardia with desaturation after balloon inflation, and the second was in relation with cardiac tamponade. Except these 2 per-procedural deaths, a significant drop in transvalvular PG was noted in all patients. This gradient fell on average from 98 ± 22 mmHg before dilatation to 32 ± 18 mmHg (p<0,001) after dilatation. Similarly, RVSP fell significantly, from 108 ± 23 to 58 ± 23 mmHg (p<0,001). Median SpO2 increased significantly from 70% IQR [50 – 84%] pre-procedural before PGE1 to 95% IQR [91-99%] post-procedural (p<0,001) (Figure 2).

At the in-hospital phase, involving 32 neonates (excluding the 2 procedural deaths): Sixteen patients (50%) required prolonged PGE1-infusion after the procedure, 7 for incomplete immediate result and 9 for non-compliant RV. Of the incomplete results, 4 were fatal and 3 early BPV-redo were performed, 2 of which were successful. Monitoring under medical treatment (PGE1 ± beta-blocker if dynamic infundibular stenosis) for an initially non-compliant RV was necessary in 10 patients, with a favorable outcome in 9 cases. Only one patient underwent early Blalock-Taussig shunt surgery after BVP-redo failure. No patient underwent DA stenting in this study. Four deaths were observed at the in-hospital phase. All deaths occurred in neonates with an incomplete BPV result, 2 with a significant residual valve stenosis and 2 with an early and significant dynamic infundibular stenosis (Figure 3).

Long-term follow-up involved 28 patients (excluding the 2 per-procedural deaths and the 4 deaths at in-hospital phase). Echocardiographic data at 12 months were available in 26 patients. A follow-up update was carried out on 31/12/2023 and concerned 24 patients with 4 patients lost to follow-up beyond 12 months. Median follow-up was 3 years IQR [1-5 years]. No deaths occurred after the hospital phase. Six late reinterventions were noted in 5 patients (18%).

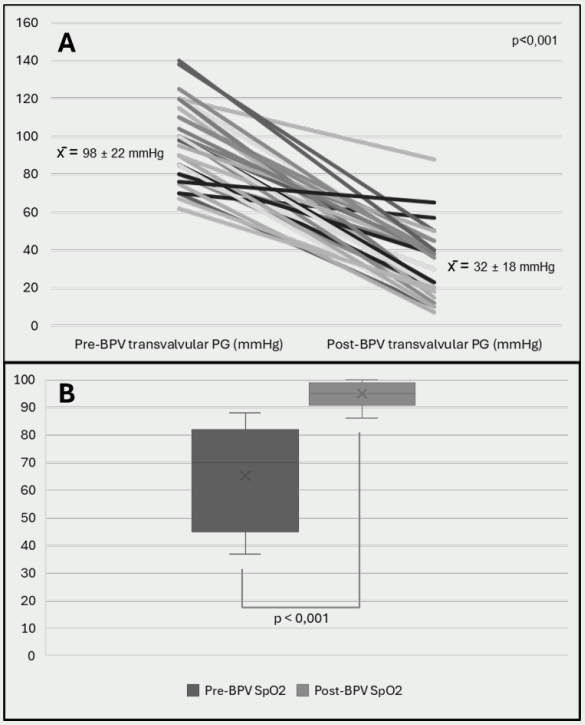

Figure 2. Panel A: Comparison of the maximum systolic transvalvular gradient before and immediately after percutaneous balloon valvuloplasty in newborns with critical pulmonary stenosis. Panel B: Comparison of pulse oxygen saturation before and after percutaneous balloon valvuloplasty in newborns with critical pulmonary stenosis.

BPV: Balloon Pulmonary Valvuloplasty, **SpO2**: Pulse Oxygen Saturation, RV/PA GrMax: Maximum systolic Right Ventricle/Pulmonary Artery transvalvular Gradient.

Five patients (18%) underwent late reintervention for RVOTO (valvular restenosis and/or fixed subvalvular restenosis) after BPV. A late BPV-redo for valvular restenosis was performed in 4 patients at 3, 3, 4 and 29 months. Surgery was required in 2 patients. The first consisted in a pulmonary valvulotomy for recurrent valvular restenosis after a late BPV-redo performed at 11 months. The second surgery was a Glenn operation (1,5 ventricles repair) associated with a foramen ovale closure for a bipartite RV was performed at 12 months. During both surgical procedures, an RV overhaul operation for fixed subvalvular stenosis was performed, allowing better bi-ventricular circulation in the first and 1,5 ventricle circulation in the second patient (Figure 3).

Freedom from death and late reinterventions at 12 months was 57.7%. Freedom from late reinterventions (among survivors to the initial BPV procedure) at 12 months was 71,4% (Figure 4).

Ultrasound data from the follow-up protocol revealed the following at 12 months (Table 2): transvalvular PG decreased significantly 1 week after BPV from 99 ± 21 to 30 ± 17 mmHg (p<0,001) and continued to decrease more slowly during the period of follow-up (35 ± 27, 35 ± 29, 24 ± 22 mmHg at 1, 6 and 12 months). Simultaneously, RVSP decreased from 107 ± 20 to 56 ± 24 mmHg 1 week after BPV (p<0.001) and continued to decrease during follow-

up (53 ± 35, 46 ± 24, 29 ± 5 mmHg at 1,6 and 12 months). Severe tricuspid regurgitation decreased significantly 1 week after BPV from 50% to 8% (p<0.05). One patient (4%) retained a grade III tricuspid regurgitation at 12 months. Moderate to severe RV hypertrophy decreased significantly from 77% before BPV to 35% of patients at 12 months (<0.05). Mean pulmonary valve annulus diameter significantly increased after BPV over the period of follow-up from 6.5±0.9 before BPV to 9.8±2 mm at 12 months (p<0.001).

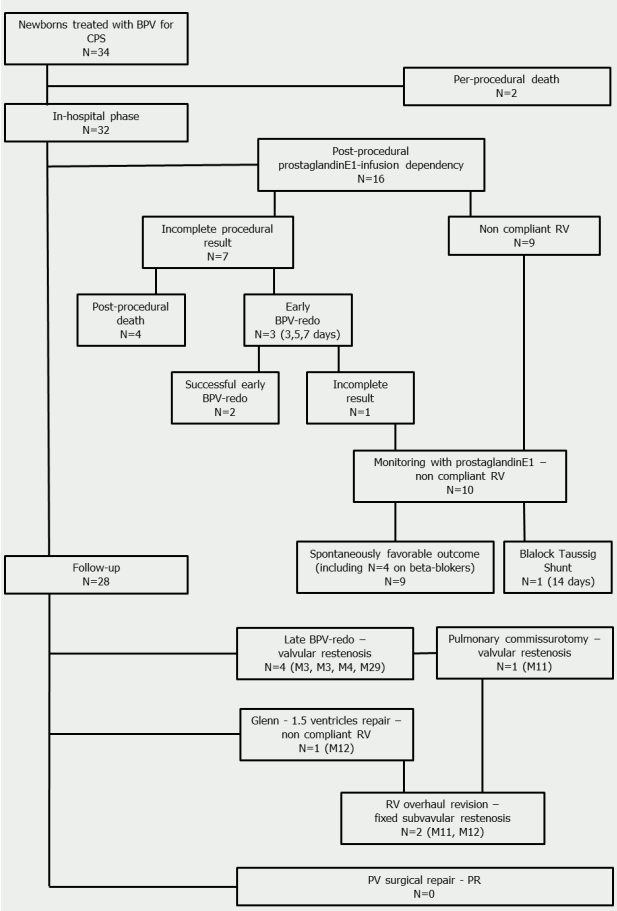

Figure 3. Early additional procedures and late reinterventions needed after balloon pulmonary valvuloplasty for critical pulmonary stenosis.

BPV: Ballon Pulmonary Valvuloplasty, **CPS**: Critical Pulmonary Stenosis, **RV**: Right Ventricle, **PR**: Pulmonary Regurgitation, **PV**: Pulmonary Valve.

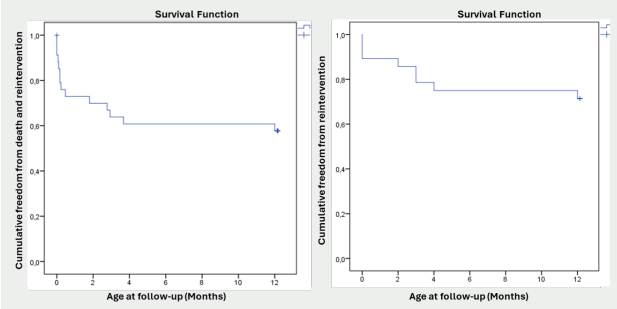

Figure 4. Kaplan-Meier curve depicting the cumulative freedom from death and late reintervention after balloon pulmonary valvuloplasty for critical pulmonary stenosis at 12 months (Left Panel). Kaplan-Meier curve depicting the cumulative freedom from late reintervention among survivors to the initial balloon pulmonary valvuloplasty for critical pulmonary stenosis at 12 months (Right Panel).

At the latest news concerning 24 patients (median follow-up was 3 years IQR [1-5 years]), all patients were eutrophic. Residual transvalvular PG was under 30 mmHg in all patients. Moderate to severe pulmonary regurgitation (PR) was observed in 11/24 patients (46%) with available long-term echocardiographic follow-up, including 3 patients (12%) with severe PR with no obvious clinical impact. No patients underwent surgical repair for PR.

Factors predicting death beyond the procedure were younger age at procedure (p=0.052), an incomplete result (p=0.006) and PGE1-infusion dependency after BPV (p=0,033).

Tachypnea (p=0.003), bipartite RV (p=0.015), incomplete result (0.033) and severe dynamic infundibular stenosis (p=0.033) were associated with the need for an additional procedure in the short-term.

Balloon/pulmonary annulus ratio was significantly smaller in patients who underwent late reintervention for RVOTO (1.12±0.17 vs. 1.33±0.17, p=0.004). In addition, a lower pre-procedural basal SpO2 was significantly associated with late reinterventions (p=0,027).

Discussion

To the best of our knowledge, this was the first African series and one of the largest international series published to date in the field of BPV for CPS of the newborn, with a median long-term clinical and echocardiographic follow-up of 3 years IQR [1-5 years]. A total of 34 newborns were included between 2000 and 2023. This retrospective descriptive study confirmed that the results of BPV for CPS in newborns were encouraging. BPV was an effective treatment for CPS in newborns, with an incompressible rate of additional early procedures related to incomplete results or a non-compliant RV, and late reinterventions often prompted by recurrent valvular or fixed subvalvular obstruction of the RVOT. Tachypnea, bipartite RV, incomplete result and severe dynamic infundibular stenosis were associated with the need for an additional procedure in the short term. Patients with lower pre-procedural basal SpO2 and a smaller balloon/pulmonary annulus ratio were more likely to undergo late reintervention for RVOTO.

Immediate results (procedural phase)

The immediate procedural success rate in our series was encouraging (73%) and was comparable to Aggarwal (77%) and Yucel (62%) series (19,21). It was significantly lower than two other recent studies of Alsawah (18) and Loureiro and al (20), where the success rate was as high as 90%. However, these two series included non-critical SPS in around 20% of their patients (18,20).

Table 2. Echocardiographic data of neonates with critical pulmonary stenosis before and after percutaneous balloon pulmonary valvuloplasty at 1, 6 and 12 months (N=26, after exclusion of 6 deceased neonates and 2 neonates with no echocardiographic follow-up available).

Variable	Pre BPV	Post BPV	1 month	6 months	12 months	p value
Transvalvular PG (mmHg)	99±21	30±17	35±27	35±29	24±22	<0.001
PVA (mm)	6.5 ± 0.9	6.5±0.9	7.3±1.1	8.5±1.3	9.8±2	<0.001
PVA Z-score	-2.08±0.90	-2.08±0.90	-1.5±1.1	-2.2±0.9	-1.9±1.3	0.74
No regurgitation	23 (88%)	13 (50%)	9 (34%)	8 (31%)	3 (12%)	0.018
PR	3 (12%)	13 (50%)	17 (66%)	18 (69%)	23 (88%)	0.034
Grade I	3 (12%)	10 (38%)	14 (54%)	14 (54%)	16 (61%)	
Grade II	0	3 (12%)	3 (12%)	4 (15%)	6 (23%)	
Grade III	0	0	0	0	1 (4%)	
Grade IV	0	0	0	0	0	
RVH	26 (100%)	26 (100%)	25 (96%)	24 (92%)	19 (73%)	0.024
Mild	2 (8%)	3 (12%)	3 (12%)	11 (42%)	10 (38%)	
Moderate	17 (65%)	18 (69%)	17 (65%)	11 (42%)	7 (27%)	
Severe	7 (27%)	5 (19%)	5 (19%)	2 (8%)	2 (8%)	
Dilated RV	13 (50%)	13 (50%)	12 (46%)	7 (27%)	5 (19%)	0.19
TVA (mm)	11±4.2	11±4.2	-	13.8±3.1	18±5.5	
TVA Z-score	0.49±4.01	0.49±4.01	-	-0.21±2.08	1.17±2.79	
No regurgitation	0	1 (4%)	2 (8%)	2 (8%)	3 (12%)	0.67
TR	26 (100%)	25 (96%)	24 (92%)	24 (92%)	23 (88%)	0.85
Grade I	5 (19%)	7 (27%)	9 (34%)	10 (38%)	12 (46%)	
Grade II	8 (31%)	16 (61%)	14 (54%)	13 (50%)	10 (38%)	
Grade III	11 (42%)	2 (8%)	1 (4%)	1 (4%)	1 (4%)	
Grade IV	2 (8%)	0	0	0	0	
RVSP (mmHg)	107±20	56±24	53±35	46±24	29±5	0.031
Dilated RA	19 (73%)	20 (77%)	20 (77%)	17 (65%)	13 (50%)	0.33
Patent FO	26 (100%)	26 (100%)	25 (96%)	25 (96%)	23 (88%)	
FO shunt						
Right-Left	22 (85%)	15 (58%)	7 (27%)	4 (15%)	2 (8%)	0.015
Left-Right	0	5 (19%)	7 (27%)	14 (54%)	16 (61%)	0.047
Bidirectional	4 (15%)	6 (23%)	11 (42%)	7 (27%)	5 (19%)	0.22
PDA	26 (100%)	24 (92%)	7 (27%)	1 (4%)	1 (4%)	
LV TSD (mm)	9.4±2.7	8.7±2.3	-	14.8±3.7	13.7 ±4.7	
LV TDD (mm)	17.4±3.5	15.3±1.2	-	22.7±3.5	23.1±7.2	
LV SF (%)	44.9±6.3	45±8.7	-	37±7.1	41.2±9.5	

BPV: Balloon Pulmonary Valvuloplasty, **LV SF**: Left Ventricular Shortening Fraction, **LV TDD**: Left Ventricle Telediastolic diameter, **LV TSD**: Left Ventricle Telesystolic Diameter, **PG**: Pressure Gradient, **PR**: Pulmonaire Regurge, **PVA**: Pulmonary Valve Annulus, **RVH**: Right Ventricular Hypertrophy, **RA**: Right Atrium, **RV**: Right Ventricle, **RVSP**: Right Ventricle Systolic Pressure, **TVA**: Anneau Tricuspid Valve Annulus, **TR**: Tricuspid Regurge.

BPV leads to an immediate drop in RVSP, with usual values between 40 and 75 mmHg, but the RVSP/systemic pressure ratio generally remains around 0.7 - 0.8 (14,15,17,20,21). In this study, RVSP after BPV was 58 ± 23 mmHg. Residual gradients in the RVOT are to be expected. In many cases, it is not possible to differentiate between a residual gradient and a gradient in the RVOT due to dynamic infundibular stenosis. RV angiography and use of an end-port catheter to measure recoil pressure can be useful in estimating the extent of obstruction at PV and subvalvular level. Residual gradients of 10-40 mmHg are common (14–21). In the current study, residual gradient was about 32 ± 18 mmHg. Most cyanotic patients experience a significant immediate increase in SpO2. However, some degree of desaturation persists in the majority of patients for some time after DA closure (6).

Short term results (in-hospital phase)

In the short term, an additional procedure may be

necessary, i.e. prolonged PGE1-infusion, more or less associated with an early reintervention consisting of an early BPV-redo, surgical pulmonary valvulotomy or surgical or endocanal shunt.
An additional procedure was required in 10 to 50% of cases in the literature, with an early reoperation rate after BPV of 5 to 40% (14–21). In our series, 50% of patients underwent an additional procedure after procedure, with an early reintervention rate after BPV of 14%. The rate of additional procedures was comparable to that reported in the literature. None of our patients underwent DA stenting, whereas use of this technique reached 38% in Yucel's series (19) and 16% in Aggarwal's series (21).

Early mortality

Early mortality rate reported in the literature following BPV for CPS varies from 0 to 14% (14–21,25). These rates are lower than those of surgery, whose rate is estimated at 20 to 25% (16). Causes of mortality are generally due to infundibular perforation with hemopericardium and tamponade or myocardial dissection occurring a few hours after the procedure (15,18,31,32).
Overall early mortality in our series was higher than that reported in the literature. A total of 6 procedural and post-procedural deaths were recorded, i.e. an early mortality rate of 18%.
Death associated factors beyond the procedure were younger age at procedure (p=0.052), incomplete results (p=0.006) and PGE1-infusion dependency after BPV (p=0,033). Additional procedures such as DA stenting or BTS may have reduced this high rate of mortality in our series. DA stenting is now an effective alternative for increasing pulmonary flow in situations of incomplete or non-compliant RV, has been under-performed in our center.
In their series, Yucel and al (19) developed a practical protocol based on SpO2 obtained after cessation of PGE1 infusion 10 minutes after BPV, as well as on RV size and morphology. If SpO2 increases, maintaining a level above 75% for 10 minutes, no additional procedure is required. If SpO2 is below 75% in patients with a hypoplastic tricuspid annulus (Z-score below -2), DA stenting is recommended during the same procedure. If SpO2 is less than 75% in patients whose RV size is considered reasonable (Z-score greater than -2), continuous infusion of PGE1 is recommended for one week to improve RV compliance. If a decrease in SpO2 (<75%) persists beyond one week, DA stenting is recommended. We propose this algorithm for the management of CPS beyond BPV, in the absence of other codifications of its management in the literature. DA stenting plays a key role among the additional procedures to be performed, as it is associated with lower morbidity and mortality. This technique makes it possible to overcome the acute phase with spontaneous occlusion of the stent, which is observed at a distance in most cases.

Long term results (beyond in-hospital phase)

In the literature, around 10 to 30% of patients with initial successful results may show signs of RVOTO (pulmonary valve restenosis with or without fixed subvalvular stenosis) within 1-2 years (6, 14–21). A late BPV-redo for pulmonary restenosis is successful in many of these patients. However, up to 10% of patients may ultimately require surgery, i.e. surgical valvulotomy in the event of failure of the late BPV-redo, a RV overhaul operation (bi-ventricular repair) or a Glenn operation (1,5 ventricle repair) in cases of associated subvalvular stenosis or a maladjusted RV (14,15,17,19–21). In this study, a total of 5 (18%) patients underwent late reintervention after BPV for CPS and freedom from reintervention in surviving patients at 12 months was 71,4%. Aggarwal had reported a reintervention-free survival rate of 65.9% (21).
Reported residual echocardiographic gradients were almost uniformly below 30 mmHg (16,20,33). Assessments have shown that both the RV and PV grow at a rate that is equal to or greater than the somatic growth rate (2,16,17,34). In most patients, BPV is the only intervention required.
After 5 to 10 years, the biggest concern is the growing importance of PR. In the literature (17–21), moderate to severe PR has been reported to be around 20 to 40% and severe PR around 4 to 10%. Moderate or even severe PR tends to remain asymptomatic for many years. Progressive dilatation of the RV was visible on echocardiography long before the onset of overt symptoms (6). Berman et al (34) found that 6/107 patients developed severe PR during a follow-up of 7.2 years. Three of these patients required PV repair and 3 others were likely to require PV replacement during childhood. Aggarwal (21) found that 22/42 patients (54%) with long-term follow-up developed moderate to severe PR during a median follow-up of 8.2. Three of these patients (7%) required PV replacement or repair. In this study, at a median follow-up of 3 years IQR [1 - 5 years], moderate to severe PR was noted 11/24 patients (46%) and severe PR in 3 patients (12%) who were asymptomatic. No PV replacement or repair was then planned.

Factors associated with recourse to an additional procedure and late reintervention

We have compared the results of our study with those of Yucel (19), Loureiro (20), and Aggarwal (21), concerning the predictive factors associated with additional short-term procedures and late reinterventions after BPV.
We demonstrated that tachypnea, bipartite RV, significant dynamic infundibular stenosis and incomplete result were significantly associated with the need for an additional procedure in the short term after BPV. Similarly to our results, Yucel (19) highlighted the importance of the presence of a bipartite RV as a robust predictive indicator. Furthermore, they demonstrated a significant correlation with a tricuspid annulus Z-score < -1.93 and a pulmonary annulus Z-score < -1.69.
Our analysis also revealed that a low preprocedural basal SpO2, as well as a lower balloon/pulmonary annulus ratio emerged as relevant predictive parameters of late reintervention for RVOTO, in line with observations in previous studies by Loureiro (20) and Aggarwal (21).

The latter also found that a smaller pulmonary annulus (pulmonary annulus z-score <-1.77) was an important factor predicting late reintervention.

Study limitations

The main limitation of our study was its retrospective data collection. The monocentric design could not give a general idea of CPS management. An extended inclusion period can be a source of bias due to evolving techniques and neonatal resuscitation practices over time but allowed recruitment of large size sample compared to published international series issued from reference centers.

Conclusion

In this series, BPV results for CPS in newborns were encouraging. Prenatal diagnosis would make it possible to schedule delivery in a level III maternity hospital close to a pediatric interventional catheterization center able to perform the only life-saving procedure: BPV. In a non-negligible proportion of cases, newborns required an additional short-term procedure. DA stenting, as an effective alternative, has been under-performed in this study. Long-term prognosis was linked to fixed valvular or subvalvular restenosis, with the noncompliant and maladjusted RV, or progression to significant PR which could necessitate late reintervention.

List of abbreviations
BPV: Balloon Pulmonary Valvuloplasty
CPS: Critical Pulmonary Stenosis
DA: Ductus arteriosus
IQR: Interquartile Range
PG: Peak-Gradient
PGE1: Prostaglandins E1
PR: Pulmonary Regurgitation
PS: Pulmonary Stenosis
SpO2: Pulse Oxygen Saturation
RV: Right Ventricle
RVOTO: Right Ventricular Outflow Tract Obstruction
RVSP: Right Ventricle Systolic Pressure

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