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Effects of balloon pulmonary valvuloplasty on longitudinal changes in right ventricular strain and strain rate in pediatric pulmonary stenosis

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Original Article

Abstract

BACKGROUND: Balloon Pulmonary Valvuloplasty (BPV) is a procedure for Pulmonary Stenosis (PS) treatment. In this study, right ventricle (RV) performance was determined through 2D-Speckle Tracking Echocardiography (2D-STE).

METHODS: The study involved 25 diagnosed children with PS undergoing BPV and 25 normal children. They were examined using 2D-STE and Linear Mixed Model (LMM) approach was used to determine changes in Pulmonary Valve Peak Gradient (PVPG), Tricuspid Annular Plane Systolic Excursion (TAPSE), strain and Strain Rate (SR) for RV, and Ejection Fraction for Left Ventricle (LVEF).

RESULTS: Notable differences were found between two groups in TAPSE ($P=0.001$), global strain ($P=0.001$), apical septal strain ($P=0.024$), middle septal strain ($P=0.001$), basal septal strain ($P=0.001$), apical lateral SR ($P=0.001$), middle lateral SR ($P=0.007$), basal lateral SR ($P=0.001$), and apical septal SR ($P=0.001$). Post-BPV, there was an increase in LVEF ($P=0.001$) and TAPSE ($P=0.001$) but PVPG decreased ($P=0.001$). Following BPV, an increase was observed in apical lateral strain ($P=0.004$), middle septal strain ($P=0.001$), apical septal strain ($P=0.003$), middle septal strain ($P=0.001$), basal septal strain ($P=0.048$), apical septal SR ($P=0.025$), and middle septal SR ($P=0.023$). Gender was remarkably correlated with mean changes in basal lateral strain ($P=0.019$), middle septal strain ($P=0.037$), and middle septal SR ($P=0.020$). Age of PS children was related to mean change in basal septal strain ($P=0.031$) and basal septal SR ($P=0.018$).

CONCLUSION: Strain and SR in RV improved post-BPV in children with PS. The gender and age of the children revealed remarkable effects on RV strain and SR changes after BPV.

Keywords: Right Ventricle; Pulmonary Stenosis; Balloon Pulmonary Valvuloplasty; Speckle Tracking Echocardiography; Pediatrics

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Introduction

Pulmonary stenosis (PS) is a benign form of congenital heart disorders, diagnosed in early infancy[1,2]. The prognosis of PS is favorable, and even children with the severe form of the disease continue their normal life after appropriate intervention[3]. PS imposes an adverse effect on the physiological performance of the heart, leading to right ventricular (RV) hypertrophy, resulting in the diminishment of right heart compliance. Moreover, PS with concurrent patent foramen oval (PFO) or atrial septal defects (ASD) may put patients at risk of right to left shunt and cyanotic condition[4,5].

Surgical valvotomy has been the main procedure for the treatment of PS until the development of balloon pulmonary valvuloplasty (BPV) by Kan et al,[6]

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which is a less invasive and appropriate treatment for moderate to severe form of valvular PS with similar results to the surgical valvotomy[7,8]. However, quantification of RV myocardial performance is crucial after BPV in PS children for the assessment of RV contraction and changes in the dimension and morphology of the RV[9].

Two-dimensional speckle tracking echocardiography (2D-STE), a relatively new method of imaging, is capable of accurately assessing regional myocardial deformation through ultrasound-based strain and strain rate (SR) parameters[10,11]. 2D-STE is an angle-independent technique that evaluates myocardial function using shorter wavelengths compared with the regular Doppler method[12]. Recently, several studies have reported 2D-STE application to evaluate ventricular function in various heart diseases, providing new information about the advantages of this method in the assessment of myocardial deformity and malfunction[13,14].

Few investigations have reported the assessment of RV performance and myocardial morphology by 2D-STE in children with PS who underwent BPV. Therefore, the authors undertook the current research to assess the effect of BPV on the RV performance by 2D-STE in children with PS and to explore the relationship between RV measures and patient characteristics.

Patients and Methods

Study design and protocol

The current prospective investigation was carried out on 25 PS children undergoing BPV and 25 normal children as control group. All procedures performed were in accordance with the 1964 Helsinki declaration, and Medical Research Ethics Committee at Isfahan University of Medical Sciences approved the study protocol (IR.MUI.MED.REC.1397.326).

Study Participants

The inclusion criteria were children with isolated PS, aged less than 18 years, and a pulmonary valve peak gradient (PVPG) > 50 mmHg. Children with concomitant heart defects and other comorbidities, the presence of supra or subvalvular PS, critical cyanotic PS, and an inadequate response to BPV based on the early residual PS (PVPG > 50 mmHg) were excluded from the study. The necessary sample size to run a linear mixed model (LMM) analysis was 25, based on the power of 90%, a type I error of 5% and a minimal clinical difference (ΔMCD) of 1.4 for mid-RV dimension before and after BPV in children with PS in the Mansour et al. study[15]. Additionally, 25 age-matched healthy children referred to the pediatric cardiac clinic for cardiology evaluation were chosen as controls.

BPV Procedure

Under general anesthesia, BPV was performed, and the percutaneous left or right femoral venous route was preferred as the catheterization entry site. A 5 to 7 Fr multipurpose catheter was inserted into the femoral vein according to the age and size of the patients and the predicted size of the balloon dilatation catheter. Following determination of the severity and site of stenosis, an exchange guidewire was introduced across the end-hole catheter and located in the distal left pulmonary artery. A Tyshak II balloon (Numed Inc., Hopkinton, NY, USA) which was greater than 20-40% of the pulmonary valve annulus size determined by angiography was located over a guidewire with the valve at its midpoint. After exchange wire stabilization, the balloon catheter was drawn back up till the middle portion of balloon was located just over the pulmonary valve. Thereafter, the balloon was fully inflated for a few seconds and quickly deflated thereafter. Repetition of inflation was done up till a sufficient decline in the gradient was observed (Figure 1).

2D-STE performance

2D-STE was performed for all subjects by a pediatric cardiology fellow with the supervision of an attending pediatric cardiologist. All patients underwent echocardiography before, one day, one month, and three months after BPV. 2D-STE was performed using an Echo 7 machine (Samsung Medison, Seoul, Korea) equipped with a 3–7 MHz probe, and the frame rate was 88 frames per second (fps). The data obtained were reviewed and analyzed prospectively on the machine by the strain software and compared to healthy children's data. Global and segmental strain and SR values for RV, including basal lateral, middle lateral, apical lateral, apical septal, middle septal, and basal septal, were obtained from the standard 4-chamber view and compared with age-matched healthy children (Figure 2). Traditional echocardiography was performed to

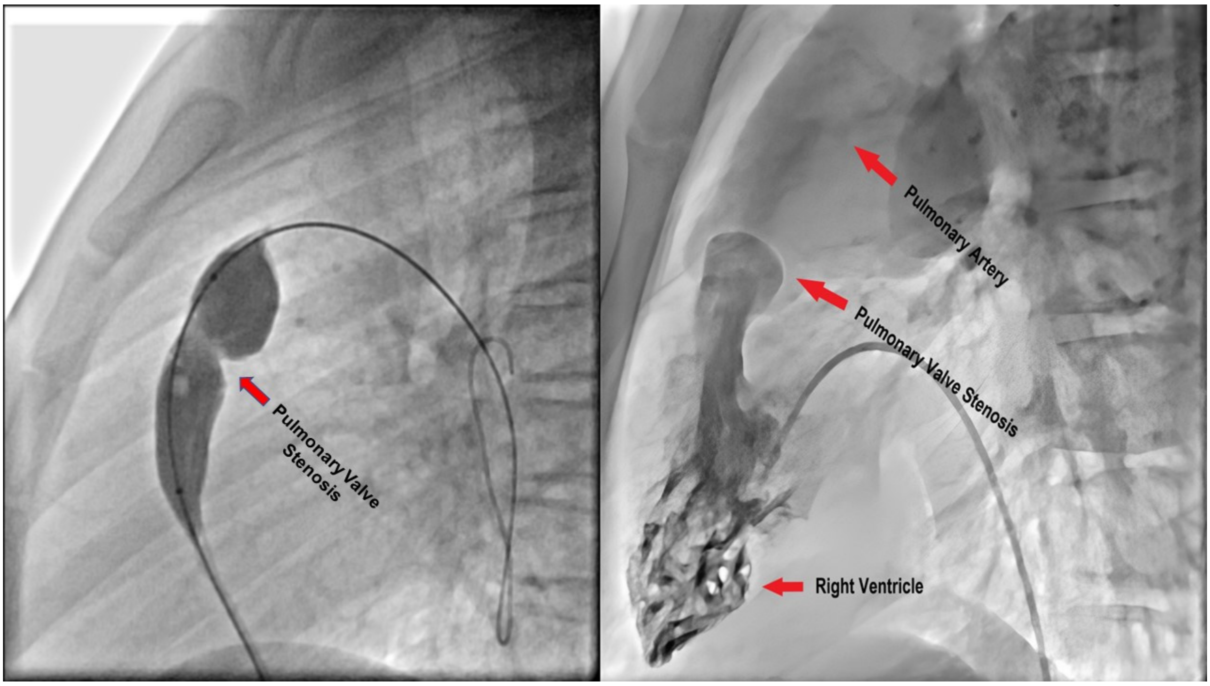

Figure 1. Lateral view of right ventricular angiogram in a 12-year-old boy (left panel) and a 14-year-old girl (right panel) representing stenotic pulmonary valve (red arrow).

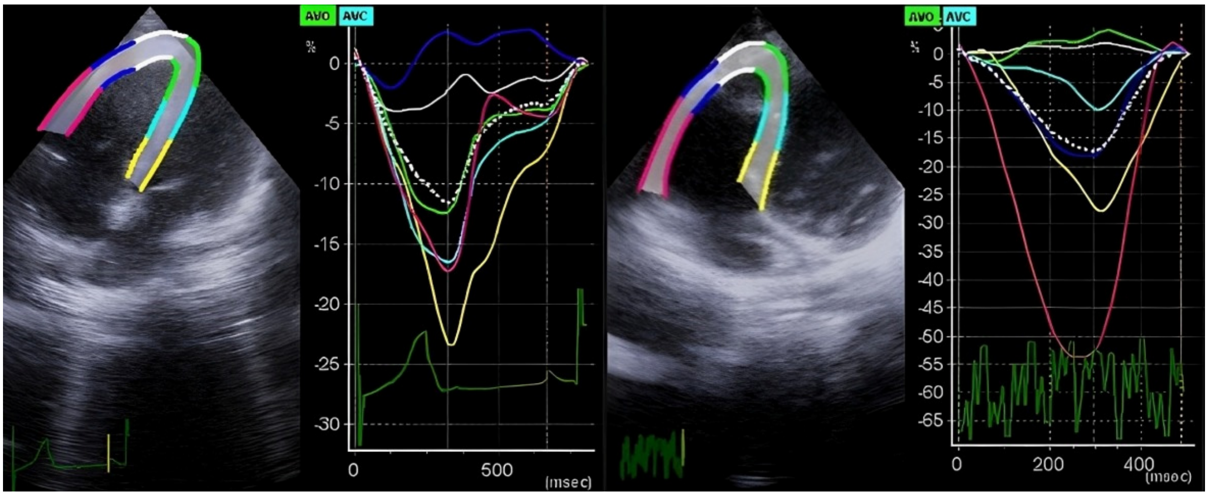

Figure 2. Right ventricular (RV) global longitudinal strain by speckle tracking echocardiography. Assessment of global longitudinal strain for RV in a child with pulmonary stenosis (strain of -11%) (left panel) and a normal child (strain of -17%) (right panel) obtained from the apical four-chamber view.

assess biventricular function via measurement of the ejection fraction for left ventricle (LVEF) and tricuspid annular plane systolic excursion (TAPSE) from the apical long-axis 4-chamber view.

Statistical Analysis

Continuous parameters are represented as mean and standard deviation (SD). Categorical parameters are presented as frequency (%). The Kolmogorov-Smirnov analysis was applied to check data normality. Categorical and continuous data were respectively compared by the chi-square test and independent t-test or Mann-Whitney test. In situations where data are correlated over more than

Table 1. Comparison of patients' variables between two groups of study

Variables	PS (n=24)	Control (n=25)	p value
Age (months) [a]	42.79±46.51	49.96±33.16	0.536
Weight (kg) [a]	15.99±9.53	17.70±6.95	0.475
BSA (m^2) [a]	0.63±0.31	0.66±0.19	0.663
Gender [b]			
Male (%)	13 (54.2%)	15 (60%)	0.680
Female (%)	11 (45.8%)	10 (40%)	

[a] Continuous data are presented as mean ± standard deviation and analyzed using student's t-test.
[b] Categorical data are presented as frequency (percentage) and analyzed using chi-squared test.
PS: pulmonary stenosis, BSA: body surface area.

two time points, LMM is used, and the authors fit LMM with terms for treatment (RV strain and SR, TAPSE, LVEF, PVPG), time (1 day, 1 month, 3 months) in PS children undergoing BPV, and the interaction between the two. Furthermore, it was assessed whether PVPG, age, gender, and weight of children were effective in longitudinal changes in RV measures. Consequently, these parameters were entered into LMM to test their effect on longitudinal changes in RV measures. Maximum likelihood with slope and intercept random effect was applied to determine all coefficients in the LMM. SPSS package (SPSS 24, Inc., Chicago, IL, USA) was used for data analysis, and a P-value was 0.05 significant if it was ≤ 0.05.

Results

Participants Characteristics

In this study, 25 diagnosed children with PS and 25 healthy children were screened and enrolled. One PS case was excluded from the final analysis due to a lack of cooperation in follow-up. Table 1 summarizes the comparison between PS children (n=24) and controls (n=25). In the PS children, there were 13 males and 11 females, whilst the healthy group consisted of 10 females and 15 males. No statistically noticeable differences were observed between the two groups regarding age, weight, and body surface area (BSA).

Comparison of Ventricular Measures in Children with PS and Controls

As shown in Table 2, the comparison of LVEF between children with PS and controls did not show a notable difference (*P*=0.626), while TAPSE in children with PS was significantly lower in comparison with normal children (*P*=0.001). Furthermore, RV global strain (*P*=0.001) and segmental strain, including apical septal (*P*=0.024), middle septal (*P*=0.001), and basal septal (*P*=0.001), were notably lower in children with PS when compared to controls. Regarding SR for RV, the authors found a significantly different value for apical lateral (*P*=0.001), middle lateral (*P*=0.007), basal lateral (*P*=0.001) and apical septal (*P*=0.001) between children with PS and controls.

Assessment of ventricular measures after BPV in PS children

As represented in Table 3, the mean LVEF (*P*=0.001) and TAPSE (*P*=0.001) increased remarkably, while a notable decrease was observed in mean PVPG (*P*=0.001) after BPV. Regarding 2D-STE parameters, apical lateral strain (*P*=0.004), middle lateral strain (*P*=0.001), apical septal strain (*P*=0.003), middle septal strain (*P*=0.001), and basal septal (*P*=0.048) showed a notable increase during follow-up for 3-month. Furthermore, a significant increase in apical septal SR (*P*=0.025) and middle septal SR (*P*=0.023) was observed over the follow-up period.

Relationship between Ventricular Measures with Variables of Treated Children

As mentioned in the statistical methodology, PVPG, gender, age, and weight of children were entered into the LMM as covariates to test their effects on mean longitudinal changes in RV measures. Results of LMM analysis in Table 4 indicated that higher PVPG in children with PS was associated with a lower change in strain value for middle lateral (β= -0.404, *P*=0.001), middle septal (β= -0.109, *P*=0.029), and apical septal (β= -0.160, *P*=0.015) over the follow-up course. Also, mean changes in middle lateral strain (β= -6.381, *P*=0.001) and basal lateral strain (β= -7.766, *P*=0.007) for male children were significantly lower when compared with females.

Table 2. Comparison of 2D-STE measures for RV between two groups of study

Variables	PS (n=24)	Control (n=25)	*P* value
Strain			
Global	-16.10 ± 5.37	-22.15 ± 2.86	0.001
Apical lateral	-17.10 ± 10.91	-13.48 ± 7.31	0.178
Middle lateral	-19.66 ± 12.0	-22.32 ± 4.13	0.302
Basal lateral	-23.26 ± 12.58	-23.74 ± 5.90	0.863
Apical septal	-15.17 ± 5.80	-9.89 ± 9.52	0.024
Middle septal	-15.32 ± 3.88	-22.70 ± 6.78	0.001
Basal septal	-19.89 ± 7.35	-37.21 ± 10.76	0.001
Strain rate			
Global	2.05 ± 0.75	2.15 ± 0.43	0.580
Apical lateral	2.77 ± 0.90	1.65 ± 1.60	0.001
Middle lateral	3.21 ± 1.83	1.79 ± 1.62	0.007
Basal lateral	3.65 ± 2.24	0.78 ± 2.59	0.001
Apical septal	2.14 ± 0.68	0.23 ± 2.22	0.001
Middle septal	2.20 ± 0.68	1.79 ± 1.91	0.324
Basal septal	2.87 ± 1.09	3.87 ± 2.51	0.079
TAPSE	14.09 ± 4.49	18.48 ± 2.77	0.001
LVEF	74.20 ± 6.48	75.16 ± 7.07	0.626

2D-STE, two-dimensional speckle tracking echocardiography; LVEF, left ventricular ejection fraction; PS, pulmonary stenosis; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.
Continuous data are presented as mean ± standard deviation and analyzed using independent student t test. $P \leq 0.05$ was considered statistically significant.

Regarding age, mean changes in strain value for global (β= 0.334, *P*=0.045), middle lateral (β= 0.661, *P*=0.001), and basal septal (β= 0.587, *P*=0.030) in older children were significantly higher, while mean changes in global SR (β= -0.036, *P*=0.050) and middle septal SR (β= -0.059, *P*=0.029) were notably lower. Moreover, higher weight was associated with a lower change in middle lateral strain (β= -0.003, *P*=0.001) and a higher change in middle septal SR (β= 0.002, *P*=0.034) during follow-up for 3 months.

Discussion

In the present investigation, the authors assessed the effect of BPV on the RV systolic function in children with PS using 2D-STE, a novel method for the quantitative assessment of global and regional myocardial function. Results of the LMM analysis in this investigation showed a time-dependent improvement in RV function after BPV in children with PS. Moreover, PVPG, gender, weight, and age of children had a notable effect on mean changes in regional RV strain and SR throughout the follow-up after BPV.

An increase in RV pressure due to PS is conveyed with multiple changes in the structure of RV, such as changes in RV morphology, movement of the interventricular septum, and ventricular hypertrophy[16]. The BPV effects on RV performance, geometry, and volumes in those suffering from congenital PS have been well-described. The measurement of RV size and performance by means of conventional echocardiography has some difficulties due to the anterior position of the RV in the chest cavity, complex asymmetrical geometry of the RV, complex crescentic shape, highly trabeculated endocardial border, the impracticability of visualizing inflow and outflow tracts simultaneously, and the lack of rational geometric models for volume measurement[17].

2D-STE-derived strain is relatively geometry-independent, less load-dependent, and angle-independent than traditional parameters for RV function, which are calculated by traditional echocardiography[18]. 2D-STE evaluates the systolic function of the ventricles by calculating the longitudinal changes of the heart muscle fibers during contraction. It has been shown that strain and SR detect changes in systolic performance before changes in ejection fraction during the development of heart disease and are useful in disorders affecting the right side of the heart[19].

Table 3. RV measures calculated by 2D-STE before and after BPV in children with PS

Variables	Before BPV	After BPV 1 day	1 month	3 months	*P* value
Strain					
Global	-16.11 ± 5.37	-17.12 ± 5.36	-17.14 ± 4.67	-18.88 ± 5.12	0.191
Apical lateral	-17.10 ± 10.91	-16.50 ± 7.13	-18.95 ± 9.44	-25.54 ± 11.35	0.004
Middle lateral	-19.67 ± 12.00	-15.64 ± 7.62	-16.47 ± 6.51	-20.76 ± 5.93	0.001
Basal lateral	-23.26 ± 12.58	-22.07 ± 9.52	-18.35 ± 8.36	-23.61 ± 11.15	0.213
Apical septal	-15.17 ± 5.80	-16.88 ± 5.46	-16.72 ± 7.90	-21.72 ± 8.25	0.003
Middle septal	-15.49 ± 3.53	-18.34 ± 5.95	-19.90 ± 6.38	-20.58 ± 5.51	0.001
Basal septal	-19.90 ± 7.35	-25.55 ± 12.40	-24.58 ± 9.60	-22.36 ± 8.65	0.048
Strain rate					
Global	2.05 ± 0.75	2.23 ± 0.87	2.24 ± 0.92	2.27 ± 0.63	0.459
Apical lateral	2.77 ± 1.65	2.53 ± 0.95	2.57 ± 0.74	2.85 ± 1.00	0.710
Middle lateral	3.21 ± 1.80	2.74 ± 1.36	2.95 ± 1.12	2.76 ± 0.86	0.570
Basal lateral	3.65 ± 2.24	3.23 ± 1.70	2.67 ± 1.03	3.00 ± 1.74	0.156
Apical septal	2.14 ± 0.68	2.40 ± 0.83	2.53 ± 0.54	2.83 ± 0.93	0.025
Middle septal	2.20 ± 0.69	2.57 ± 1.28	2.90 ± 1.40	2.78 ± 1.26	0.023
Basal septal	2.87 ± 1.10	3.66 ± 1.84	3.56 ± 1.63	3.25 ± 1.50	0.106
TAPSE	14.10 ± 4.49	14.01 ± 4.57	14.52 ± 4.37	14.93 ± 4.56	0.001
LVEF	74.20 ± 6.48	74.30 ± 4.57	74.33 ± 4.51	77.09 ± 2.72	0.001
PVPG	70.12 ± 13.81	38.83 ± 17.92	41.29 ± 14.93	45.17 ± 14.48	0.001

2D-STE, two-dimensional speckle tracking echocardiography; BPV, balloon pulmonary valvuloplasty; LVEF, left ventricular ejection fraction; PS, pulmonary stenosis; PVPG, pulmonary valve pressure gradient; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.
Continuous data are presented as mean ± standard deviation and analyzed using linear mixed model analysis. P <0.05 was considered statistically significant.

The results of 2D-STE in this study revealed that RV regional and global strain in children with PS is significantly lower than in control children, suggesting impaired RV systolic function in these patients. However, the increase in regional strain and SR after BPV in PS may be due to changes in the RV dimension, regression in the RV thickness, noticeable RV mass improvement, and interventricular septal bowing[15]. It is postulated that following relief of RV pressure, the enlarged RV regains its normal elongated geometry in preference to the globular shape[20]. Fukui et al. reported RV reverse remodeling quantified by cardiac magnetic resonance (CMR) imaging following balloon pulmonary angioplasty in individuals with chronic thromboembolic pulmonary hypertension[21]. Furthermore, RV and LV systolic performance in the present study significantly improved three months after BPV, as manifested by improved TAPSE and LVEF in children. The current findings are in parallel with those of Agha et al. [22] and Mahfouz et al.,[20] who reported a significant improvement in RV growth and performance after BPV for critical PS in children.

Limitations

This investigation has some limitations. Firstly, we ran a single-center study and our main limitation was the relatively small number of children. Therefore, a multicenter study with a larger population and longer follow-up period is proposed. Secondly, RV function was evaluated only based on changes in longitudinal strain derived from 2D-STE. Radial and circumferential strain, RV torsion, and synchrony were not examined. Lastly, further comprehensive studies are necessary to assess RV performance more precisely through quantifying fractional area change

Table 4. Effects of PVPG, gender, age, weight of PS children on RV measures after BPV during 3 months follow up

RV measures	PVPG		Gender		Age		Weight	
	β	*P* value	β	*P* value	β	*P* value	β	*P* value
Global strain	-0.091	0.133	-0.973	0.571	0.334	0.045	-0.001	0.079
Global SR	0.005	0.386	-0.152	0.427	-0.036	0.050	0.001	0.104
Apical lateral strain	0.001	0.987	3.642	0.246	0.045	0.873	3.825	0.978
Apical lateral SR	0.004	0.580	-0.112	0.660	-0.013	0.570	5.190	0.655
Middle lateral strain	-0.404	0.001	-6.381	0.001	0.661	0.001	-0.003	0.001
Middle lateral SR	0.037	0.143	0.740	0.223	-0.069	0.217	0.003	0.234
Basal lateral strain	-0.085	0.352	-7.766	0.007	0.415	0.097	-0.001	0.110
Basal lateral SR	0.016	0.278	0.680	0.123	-0.038	0.335	0.001	0.422
Apical septal strain	-0.160	0.015	1.889	0.291	0.093	0.565	-0.003	0.627
Apical septal SR	0.110	0.169	-0.101	0.627	-0.013	0.494	4.885	0.608
Middle septal strain	-0.109	0.029	1.766	0.205	0.258	0.051	-0.001	0.076
Middle septal SR	0.003	0.681	-0.446	0.119	-0.059	0.029	0.002	0.034
Basal septal strain	-0.063	0.511	-1.083	0.697	0.587	0.030	-0.002	0.059
Basal septal SR	-0.005	0.699	0.264	0.491	-0.069	0.061	0.002	0.122
TAPSE	0.030	0.672	0.592	0.775	-0.168	0.381	0.008	0.356
LVEF	0.062	0.222	-0.621	0.667	0.040	0.761	-0.002	0.659

BPV, balloon pulmonary valvuloplasty; LMM, linear mixed model; LVEF, left ventricular ejection fraction; PVPG, pulmonary valve pressure gradient; RV, right ventricle; SR, strain rate; TAPSE, tricuspid annular plane systolic excursion. *P* value ≤ 0.05 is significant.

(FAC), RV end-diastolic area (RVEDA), and RV end-systolic area (RVESA).

Conclusion

RV global and regional performance improved in children with PS following successful BPV, providing valuable insight for early intervention in children suffering from PS to prevent development to permanent RV deformation and failure. Moreover, strain and SR quantified by 2D-STE can be used in children as appropriate and useful parameters in the assessment of regional and global RV function in PS following treatment with BPV.

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Conflict of Interest

The authors declare no conflicts of interest.

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Authors' Contribution

All authors made substantial contributions to the conception and design of the study or data acquisition, analysis, or interpretation. All authors reviewed and approved the final manuscript. Davood Ramezani Nezhad and Mohsen Sedighi take full responsibility for the integrity of the submission and publication and were involved in the study design.

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