

3D Echocardiographic Evaluation of Right Ventricular Functions: A Prognostic Study in Pediatric Population with Critical Pulmonary Stenosis Undergoing Balloon Pulmonary Valvuloplasty

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ABSTRACT

Background: Critical pulmonary stenosis has been associated with severe right ventricular outflow tract obstruction (RVOTO) leading to severe right ventricular hypertrophy (RVH), impaired both systolic and diastolic functions, changes in RV shape and geometry, hence further assessment by 3D echocardiography (3D Echo) is recommended.

Objective: The aim of the current work was to evaluate RV (Right Ventricle) functional indices using 3D echocardiography in infants with critical pulmonary stenosis undergoing balloon pulmonary valvuloplasty and to evaluate RV (Right ventricle) indices as follow up parameters in infants with critical pulmonary stenosis (PS).

Patients and Methods: This prospective study included a total of 60 infants with critical pulmonary stenosis, their median age was 8.5 (range 2 - 12) months referred for urgent balloon pulmonary valvuloplasty to Pediatric Cardiology Unit, Department of Cardiology, Ain Shams University Hospitals.

Results: 3D echo revealed lower RV (Right ventricle) volumes ($P < 0.001$), higher FAC (fractional area change) ($P < 0.001$), higher TAPSE (tricuspid annular plane systolic excursion) ($P < 0.001$), higher EF (Ejection fraction) ($P < 0.001$), lower basal, mid and longitudinal RV dimension ($P < 0.001$). FAC (fractional area change), TAPSE (tricuspid annular plane systolic excursion) and RV basal and longitudinal diameter were significantly larger by 3-dimensional echocardiography (3D Echo) than by 2-dimensional echocardiography (2D Echo) ($P = 0.01$).

Conclusions: It could be concluded that in patients with critical pulmonary stenosis undergoing balloon pulmonary valvuloplasty, assessment of RV indices using 3 D echo is more reliable and effective method to assess RV volumes and function in comparison with conventional 2D echocardiography.

Keywords: 3D echo, Critical pulmonary stenosis, Balloon pulmonary valvuloplasty, RV functions.

INTRODUCTION

Critical Pulmonary Stenosis (CPS) is a life threatening condition due to severe RVOT obstruction with RV pressure that exceeds systemic pressure, commonly presents in the neonates and infants with cyanosis due to reversal of flow across the patent foramen ovale (PFO) or atrial septal defect (ASD), patients usually have PDA dependent pulmonary circulation and urgent catheter intervention is needed⁽¹⁾.

Critical pulmonary stenosis has been associated with severe RVOT obstruction leading to severe RV hypertrophy, impaired both systolic and diastolic functions, changes in RV shape and geometry. After balloon pulmonary valvuloplasty, early removal of RVOTO helps in reverting the unfavorable effects of pressure overload on RV⁽²⁾.

Accordingly, echocardiography plays a major role in diagnosis, assessment and management of critical pulmonary valve stenosis. It is helpful for detecting the degree of stenosis (pressure drop across the pulmonary valve), level of obstruction (sub-valvular, valvular or supra-valvular), associated intracardiac anomalies and the proper management strategy. Assessment of RV volumes and systolic functions are important determinants of the outcome of the intervention, which cannot be assessed accurately by 2D echo using Simpson's method due to the triangular shape of the RV which makes it difficult to visualize it all in one view and hence limits the role of 2D echo⁽³⁾, the RV is heavily trabeculated with prominent moderator and peculiar arrangement of its fibers in two perpendicular directions: longitudinally (RV inflow)

and circumferentially (RV outflow). Because of this unique RV morphology, 2D echo has several limitations in the evaluation of RV⁽⁴⁾.

Three-dimensional echocardiography (3DE) provides wide gated complete acquisition which enables complete assessment of RV volumes, morphology and ventricular functions. 3D echo has the ability to display the surfaces of entire RV including the inflow, trabecular and outflow portion. 3D echo allows us to measure RV end-diastolic volume, RV end-systolic volumes and ejection fraction (RVEF) regardless of its shape and evaluate the morphologic and functional remodeling of the RV in patients with critical PS⁽⁴⁾. Several clinical studies have shown a good correlation between cardiac magnetic resonance (CMR) and 3DE derived volumes and ejection fraction of the RV in selected population with most studies showing slight underestimation of volumes when compared with those measured by CMR. The aim of the current work was to evaluate RV (Right Ventricle) functional indices using 3D echocardiography in infants with critical pulmonary stenosis undergoing balloon pulmonary valvuloplasty and to evaluate RV indices as follow up parameters in these infants.

PATIENTS AND METHODS

This prospective study included a total of 60 infants with critical pulmonary stenosis, their median age was 8.5 (range 2 - 12) months, referred for urgent balloon pulmonary valvuloplasty to Pediatric Cardiology Unit, Department of Cardiology, Ain Shams University Hospitals.

Inclusion criteria:

- Patients less than 1 year of age with critical pulmonary stenosis (defined as RV pressure RV pressure equal to or greater than systemic pressure) regardless of symptoms, valve morphology, associated hemodynamically insignificant congenital cardiac lesions such as atrial septal defect (ASD), small ventricular septal defect (VSD), patent foramen ovale (PFO), patent ductus arteriosus (PDA)
- Patients with critical PS causing severe cyanosis due to reversal of shunt across PFO
- Patients with critical PS associated with RV dysfunction or with hemodynamics instability.

Exclusion criteria:

- Patient with previous balloon pulmonary valvuloplasty.
- Patient with other hemodynamically significant congenital cardiac defects, e.g., hemodynamically significant shunts as large ASD, large VSD or large PDA.
- Insufficient ultrasound image quality (defined as more than 3 myocardial segments that were not optimally visualized using conventional 2DE).
- Any contraindication to cardiac catheterization.

After full history taking (with especial emphasis on gestational and natal history, history of cyanosis, weight gain and development, failure to thrive manifestations of heart failure) and clinical examination (with especial emphasis on general examination as complexion as cyanosis, tachypnea, tachycardia, intercostal retractions and local cardiac examination in the form of ejection systolic murmur over upper left sternal border, ejection click) followed by echocardiographic evaluation by both conventional 2D echo and 3D echo for head to head comparison before, 24 hours after BPV and 6 months in the follow up.

2D echocardiography:

A Full 2D echo study was carried out using GE vivid E9 echocardiography machine with phased array transducers. Using both M5 and 6S probes. sequential segmental analysis was done in all echocardiographic views including (parasternal long and short axis, apical 4, 2 and 5-chamber, subcostal and suprasternal views) in addition to color Doppler and continuous-wave Doppler. RV assessment was done as follows : assessment of RV wall thickness, RA area, color and continuous wave doppler to assess the level and severity of stenosis, localized PR and its grading, leaflet morphology and thickening, assessment of pulmonary valve for (dysplasia, hypoplasia, post stenotic dilatation, branch pulmonary stenosis), assess for PDA and duct dependent pulmonary blood flow, assess for PFO or ASD, PV annulus according to Z-score with especial emphasis on assessment of RV functions as fractional area change (FAC) and TAPSE in addition to assessment of LV functions and flattening of IVS during diastole.

3D echocardiography:

- 3D echo was done before balloon pulmonary valvuloplasty and repeated within 24 hrs after the procedure then after 6 months later to assess the Impact of balloon pulmonary valvuloplasty on RV quantification. It was done using a dedicated wide-angle, broadband X7-1 (Vivid E9) matrix-array transducer to allow for full cover of the entire RV by the pyramidal volume, with special attention to the outflow tract. All 3D echocardiographic measurements were done once by a single operator using the multiple-beat 3D acquisition which acquires narrow volumes of information over several heart beats ranging from 4-7 cardiac cycles that are stitched together to create a larger volumetric data set, this method of data set acquisition compensates for the poor temporal resolution of single beat full volumetric real-time 3DE acquisition. Before acquisition, images were optimized for the endocardial border visualization, modifying overall gain and adjusting time gain and compression with frame rate adjusted from 15-20 Hz. Then they were digitally stored for offline analysis by the available software (4DAuto RVQ, Echo Pac software v202). Then the 4D auto RV quantification was done by offline analysis after obtaining clear RV focused view to align the views, set the landmarks and adjusting of the RV contours then the software automatically provides the 3D reconstruction model and all the following data were obtained: 3D EDVI, 3D ESVI, 3D EF, 3D SV, 3D model of RV.

Ethical consent:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Ain Shams University. Written informed consent was taken from the participants' parents. The study was conducted according to the Declaration of Helsinki.

Statistical analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data with parametric distribution were presented as mean, standard deviations and ranges while with non parametric were presented as median with inter-quartile range (IQR). Also qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test when the expected count in any cell found less than 5. The comparison between more than two paired groups with quantitative data and parametric distribution was done by using Repeated Measures ANOVA followed by post hoc analysis using Bonferoni while with non-parametric distribution were done by using Freidman test followed by post hoc analysis using Wilcoxon Rank test. The comparison between two independent groups with quantitative data

and parametric distribution was done by using independent t-test while with non-parametric distribution were done by using Mann-Whitney test. P value < 0.05 was considered significant.

RESULTS

The study included 38 males (63.3%) and 22 females (36.7%) with a median age of 8.5 months (ranged from 2 months to 12 months), with body weight ranged from 5 kg to 39 kg with a median of 9.5 kg. as shown in table 1.

Table (1): Demographic data of the infants with critical pulmonary stenosis.

		No. = 60
Age (months)	Median (IQR) Range	8.5 2 – 12
Sex	Female Male	22 (6.7%) 38 (63.3%)
Weight (KG)	Median (IQR) Range	9.5 (7 – 22.25) 5 – 39
Height (cm)	Mean ± SD Range	88.76 ± 30.39 58 – 145
BSA (m ²)	Mean ± SD Range	0.60 ± 0.31 0.29 – 1.25

2 D echocardiographic assessment:

The following parameters were assessed before, within 24 hrs. and 6 months after the procedure: pressure gradient across the valve, RV wall thickness, right atrial area indexed, PV annulus diameter, RV longitudinal and basal diameter, FAC (fractional area change) and TAPSE (tricuspid annular plane systolic excursion) in addition to LV ejection fraction.

It was found that PV annulus and RA area indexed were reduced significantly after 6 month follow up in comparison to before and within 24 hrs. after the BPV (P- value <0.01, <0.01) respectively. only the RV basal diameter significantly reduced only in the 6 months follow up (P value 0.01) while the RV longitudinal diameter was not significantly reduced in the follow up, both in comparison to before the BPV (P value = 0.06), while PG across the PV, FAC and TAPSE were significantly reduced within 24 hrs, and in the 6 months follow up (P Value < 0.01) for each in comparison to before the BPV, in addition to the LV EF was not significantly increased in the 6 months follow up as shown in the table (2).

Table (2): Assessment of 2D echocardiographic parameters.

EDVI (end diastolic volume indexed), ESVI (end systolic volume indexed), TAPSE (trans-annular systolic plane

Three dimensional echocardiography		Before BPV No. = 60	After BPV No. = 60	6 month follow up No. = 60	P-value
EDV I ml/m ²	Mean ± SD Range	24.3 ± 5.43 11.7 – 94.8	24 ± 5.41 11 – 94	21.6 ± 4.83 10.4 – 92.7	0.000
ESV I ml/m ²	Mean ± SD Range	13.45 ± 3.12 5.7 – 59.7	13.2 ± 2.82 5 – 59.4	12.35 ± 2.72 5.7 – 58.7	0.000
RV EF %	Mean ± SD Range	41.27 ± 9.16 23.8 – 57.1	52.37 ± 7.51 40 – 65.9	54.53 ± 6.78 42 – 67.8	0.000
Basal RV dimension mm	Mean ± SD Range	28.90 ± 9.30 16 – 47	27.80 ± 9.06 16 – 50	25.15 ± 8.70 17 – 49	0.000
Longitudinal RV dimension mm	Mean ± SD Range	35.17 ± 8.21 15 – 57	42.95 ± 10.00 25 – 78	47.82 ± 9.85 26 – 79	0.000
TAPSE mm	Mean ± SD Range	9.19 ± 2.07 6 – 14.9	12.02 ± 3.05 7 – 19	13.79 ± 2.97 8 – 21	0.000
FAC %	Mean ± SD Range	39.50 ± 8.01 24.2 – 59	48.00 ± 7.47 30.3 – 64.1	51.07 ± 7.33 33.7 – 66.6	0.000
LV EF	Mean ± SD Range	65.25 ± 9.02 57- 74	66.275 ± 8.30 56-75	66.35 ± 8.88 56- 76	0.534

excursion), FAC (fractional area change).

3D echocardiographic assessment:

3D derived RV volumes, RV longitudinal and basal diameter, EF, TAPSE, FAC were assessed before, within 24 hours and after 6 months in the follow up. The following results were obtained. both RV EDVI and ESVI only significantly decreased in the 6 months follow up in comparison to that obtained before and within 24 hours after the BPV (with median of 21.6 (15.33-32.3) ml/m² and median of 12.35 (8.85-26.55) ml/m² P value < 0.01) respectively.

While 3D derived EF, TAPSE and FAC were significantly increased within 24 hrs and in the 6 months follow up in comparison to the preprocedural parameters as follows : 3D derived EF increased from a mean of 41.27% ±9.16% before BPV to a mean of

52.37%±7.51% within 24 hours after BPV (P<0.05) and also it increased to a mean of 54.53% ± 6.78% at 6 months in the follow up (P<0.01), 3D derived TAPSE increased from a mean of 9.19mm ± 2.07mm before BPV to a mean of 12.02 mm ± 3.05 mm within 24 hours after BPV (P<0.05) and also it increased to a mean of 13.79 mm ± 2.97 mm after 6 month (P<0.01), 3D derived FAC increased from a mean of 39.5% ± 8.01% before BPV to a mean of 48% ± 7.47% within 24 hours BPV (P<0.05) and also it increased to a mean of 51.07% ± 7.33% in the 6 month follow up (P<0.01), while the RV basal diameter was significantly reduced in the 6 months follow up(p value <0.01), and RV longitudinal diameter was significantly increased in the 6 months follow up (P value < 0.01) as shown in table 3.

Table (3): Three-dimensional echocardiographic measurement before, immediately after BPV and at 3-6 month follow up.

	Post Hoc analysis		
	Before BPV VS After BPV immediately P value	Before BPV VS 3-6 month follow up P value	After BPV immediately VS 3-6 month follow up P value
EDV I	0.536	0.000	0.000
ESV I	0.291	0.000	0000
RV EF	0.000	0.000	0.000
Basal RV dimension	0.000	0.000	0.000
Longitudinal RV dimension	0.000	0.000	0.000
TAPSE	0.004	0.000	0.000
FAC	0.003	0.000	0.000

EDVI (end diastolic volume indexed), ESVI (end systolic volume indexed), TAPSE (trans-annular systolic plane excursion), FAC (fractional area change).

3D echo versus 2D echo assessment of the RV indices:

On comparing the RV dimensional and functional parameters measured by 2D and 3D echo. firstly the RV functional parameters as FAC and TAPSE as assessed 24 hours and 6 months after the BPV, were significantly larger by 3d echo than those obtained by 2D echo (P=0.01) as shown in figure 1, 2 and table 4. Also the RV dimensions (RV basal and longitudinal diameter) when assessed by 3D echo were statistically larger when compared with those obtained by 2D echo (P=0.01) as shown in figure 2, table 4. Linear analyses showed that values of conventional 2D images were well correlated with those of 3D images. Table 4.

Table (4): Correlation between three dimensional ECHO and two dimensional ECHO in terms of RV basal diameter, RV longitudinal diameter, TAPSE and FAC:

	2D echo 6 months after BPV	3D echo 6 months after BPV	R	P value
TAPSE	10.55 ± 2.45	13.79 ± 2.97	0.670519	0.005
FAC	47.15 ± 6.32	51.07 ± 7.33	0.621562	0.005
RV basal diameter	22.65 ± 5.40	25.15 ± 6.21	0.678932	0.001
RV longitudinal diameter	44.52 ± 7.55	47.82 ± 9.85	0.645321	0.001

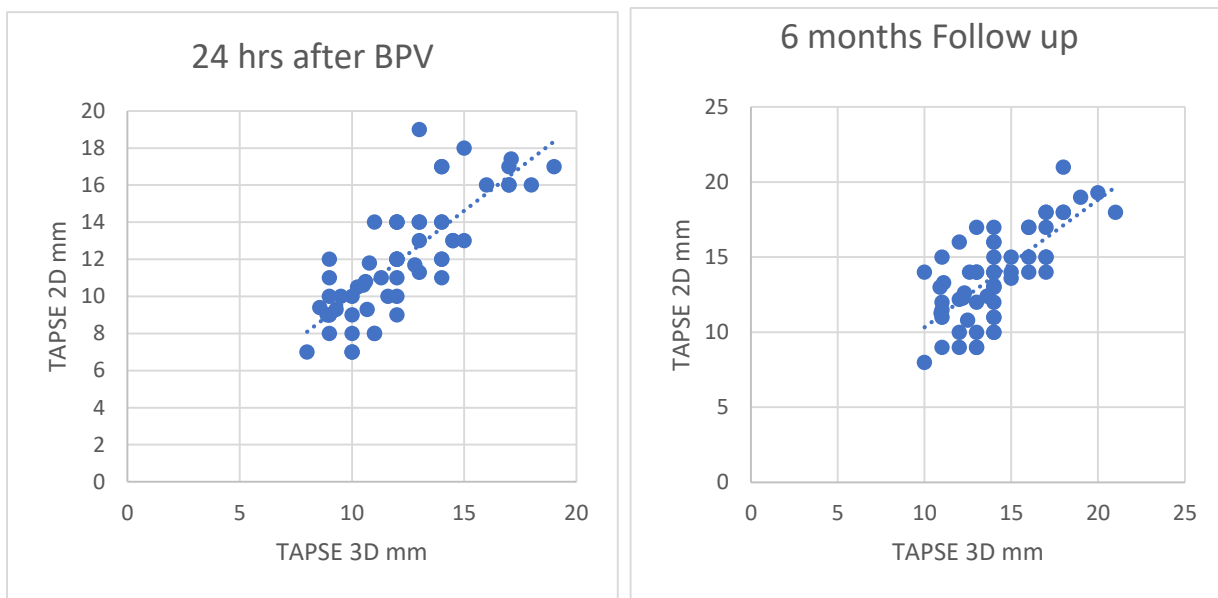


Figure (1): Correlation between 2D and 3D Echo regarding TAPSE 24 hours after BPV and 6 months follow up

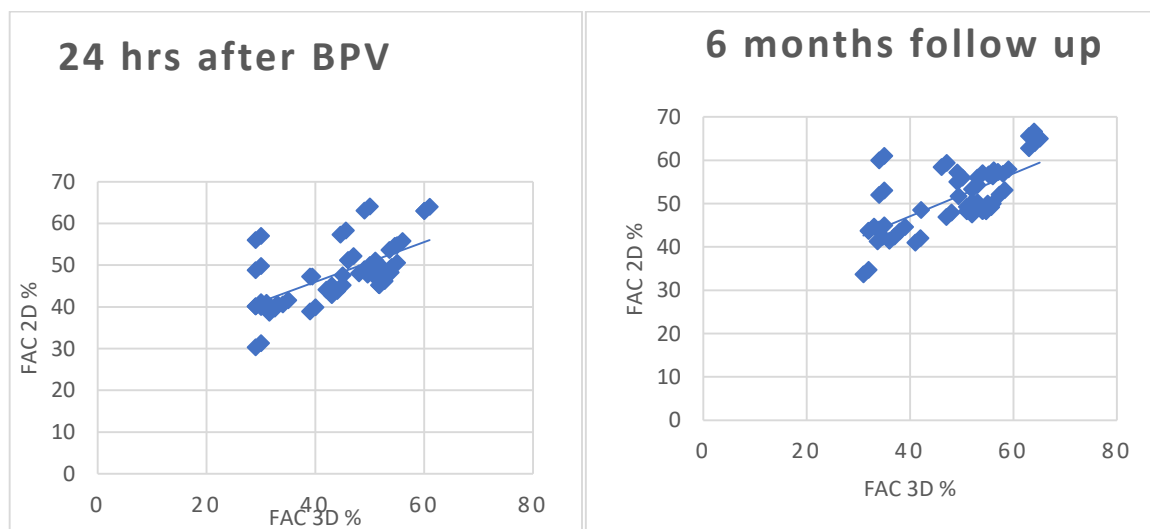


Figure (2): Correlation between 2D and 3D Echo regarding FAC 24 hours after and 6 months follow up.

DISCUSSION

The aim of this study was to identify role of 3D echocardiographic in comparison to conventional 2D echo in assessment of RV volumes and function in infants with critical pulmonary stenosis undergoing balloon pulmonary valvuloplasty pre and post dilatation, and to evaluate these indices as follow up parameters for the procedural success.

Neonates and infants with critical pulmonary stenosis with significant RV pressure load directly affects RV shape, volumes, functions, and morphology with consequent changes in these parameters after balloon pulmonary valvuloplasty ⁽⁴⁾.

In contrast to the LV the RV is an anterior complex asymmetrical structure which makes its assessment limited by the 2D echo in addition to inability to visualize both its inflow and outflow portion in the same view and the heavily trabeculated myocardium which makes it difficult to track the endocardial border and consequently quantification of RV volumes and function using conventional echo is challenging and lacking accurate assessment ⁽⁵⁾.

Accordingly, and despite that numerous 2DE quantitative methods based on geometric postulations have been established, for better quantifying of the RV shape and functions, however it still poses a big challenge ^(6, 7). 3D echocardiography has become more useful in diagnosis and management of congenital heart disease (CHD) patients, particularly before surgical intervention or cardiac catheter intervention. 3D echocardiography has been used recently in patients with congenital heart disease because of better acoustic window and the non-invasive assessment using this technique ⁽⁸⁾. 3 DE is currently gaining attention and familiarity as a more accurate and reproducible modality for RV evaluation especially on congenital and structure heart disease ⁽⁹⁾.

The current study included 60 patients with critical pulmonary stenosis who were referred for right ventricular function evaluation by 2-dimensional (2DE) and 3-dimensional echocardiography (3DE) before & immediately after BPV, and at 6 month follow up in the Cardiology Department, Ain Shams University Hospitals.

The current study it was found that RA area indexed, and PV annulus were significantly reduced in the 6 month follow up which was comparable to the results with the study of **Agha et al.** ⁽¹⁰⁾, stating that right heart structures improved gradually and started to grow significantly after 3-6 months of BPV.

We also noticed that TAPSE and FAC were significantly increased within 24 hours after, and in 6 months follow up, which were comparable with study of **Fukui et al.** ⁽¹¹⁾ which demonstrated that RV EDVi and ESVi markedly improved with concomitant increase in RV EF and FAC. While **Agha et al.** ⁽¹⁰⁾ reported that TAPSE significantly improved immediately and in the 3-6 months follow up.

We reported that 3D derived RV EDVI and RV ESVI were significantly decreased in the 6 months follow up from a median of 12.35(8.85-26.55) ml/m² and 21.6(15.33-32.3) ml/m². These results were nearly agreed with **Fukui et al.** ⁽¹¹⁾, who demonstrated that the RV EDV and RV ESV indexed are markedly improved after BPA in CTEPH patients.

Similarly both 3D RV EF and TASPE were increased significantly within 24 hours after and in the 6 months follow up as follows (RV EF increased from 41.27% ±9.16% before BPV to a mean of 54.53% ± 6.78% at 3-6 month follow up, while RV TAPSE increased from a mean of 39.5% ± 8.01% before BPV to a mean of 51.07%±7.33% at 3-6 months follow up, which was concur with the study of **Tsugu et al.** ⁽¹²⁾ which showed a significant improvement in RVEF in

patient with CTEPH after balloon pulmonary angioplasty, also our results were similar to results published by **Moriyama et al.** ⁽¹³⁾ when they studied the effect of pressure overload reduction on the RV EF and TAPSE by 3D echo in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

In our study we also noted that 3D derived RV longitudinal diameter increased significantly in the 6 months follow up while RV basal diameter decreased significantly in the 6 months follow up which could be explained as the anatomy of the RV has a more complex asymmetrical geometry being wrapped around the LV, as the specific arrangement of RV myocardial fibers as the epicardial fibers are arranged obliquely in contiguous with the LV fibers and the endocardial fibers are arranged longitudinally ⁽¹⁴⁾, which makes the RV increase in the circumferential diameter rather than the longitudinal diameter with increased RV pressure load, on relieving the RV pressure the dilated RV regains its normal elongated geometry (i.e decrease in the circumferential dimension and increase in the longitudinal dimension) rather than globular shape. In study done by Fernandez **Friera et al.** ⁽¹⁵⁾ noticed that there were regional differences between the RV segments where the basal segments showed better contractility than others and this is mostly due to variation in the pressure load which affects segments rather than others. In study done by **Dambrauskaite et al.** ⁽¹⁶⁾ they observed apical to basal difference in deformation and deformation rate which can be explained by: Firstly, longitudinal deformation is smaller in structures with straight walls, which can be seen in patients with long standing pulmonary hypertension as apical segments are less affected. Secondly, passive wall stress is also higher when the wall is thin, as in the apical segment of the RV free wall, **Anderson and Becker** ⁽¹⁷⁾. Thirdly, in Pulmonary hypertension RV remodeled the deformation in the apical segments may be decreased due to the different embryonic origin of the RV or due to difference in the distribution of adrenergic receptors which is more located in the RV base rather than the apex **Pierpont et al.** ⁽¹⁸⁾.

In our study on comparing the RV dimensional and functional parameters measured by 3D echo versus 2D echo, FAC, TAPSE, RV basal and longitudinal diameters were significantly higher and accurately assessed by 3D echo than those measured by 2D echo these results were in concur with study of Van der Zwaan *et al.* ⁽¹⁹⁾ which stated that 3D echo shows better quantitative RV volumes and function assessment compared with 2D echo in patients and in healthy controls.

Also 3D derived FAC, TAPSE and RV geometry serve as an outcome predictors for pediatric patients with RV pressure overload (infants with critical pulmonary stenosis) this was also reported by Jone *et al.* ⁽²⁰⁾ where 3D RV EF, volumes, FAC, and free wall RV strain serve as outcome predictors for pediatric pulmonary hypertension patients. So because of the RV peculiar morphology and functions, 2D echo has several limitations in the evaluation of right ventricle which can be overcome by 3D echo gated wide angle acquisition, which enable complete assessment of its geometry, volumes and ejection fraction.

LIMITATIONS

The current study is a single center study, only focused on immediate and intermediate term procedural outcomes. In the future we hope to complete a multicenter study with larger sample sizes and long term follow up.

CONCLUSIONS

It could be concluded that in patients with critical PS undergoing BPV, assessment of RV indices using 3D echo is more reliable and effective method to assess RV volumes and function in comparison with conventional 2D echocardiography. 3D derived RV volumes, RV EF, TAPSE and FAC can be used for accurate follow up for patients with critical pulmonary stenosis undergoing BPV.

Financial support and sponsorship: Nil.

Conflict of interest: Nil.

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