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**Pediatric** 

# **Original Article**

Speckle Tracking Echocardiographic Ventricular Functions In Infants With Pulmonary Hypertension With Shunt Disease

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#### **ABSTRACT**

Background: Pulmonary arterial hypertension (PAH) is a common complication of congenital heart disease (CHD), with most cases occurring in patients with congenital cardiac shunts with increased morbidity and mortality. **Objectives**: This study aimed to assess the right and left ventricular functions and their strain pattern among infants with pulmonary hypertension associated with shunt disease by 2-D speckle tracking echocardiography and correlate these finding with haemoynamic, clinical and echocardiographic findings among such patients. Patients & Methods: This study was carried out at the Pediatric Cardiology Unit, Pediatric Department, Zagazig University Hospital, during the period from June 2018 till February 2019. Results: In our study, it was found that Pulmonary artery systolic pressure values among infant with pulmonary hypertension with shunt is a strong positive predictors of Average LV Circumferential strain value. There were statistically significant differences between patients with moderate and severe pulmonary hypertension as regard their RVGLS. Conclusions: Twodimensional speckle-tracking echocardiography is a complementary noninvasive tool for assessment of right and left ventricular function in children with pulmonary arterial hypertension, allowing analysis of both segmental and global (longitudinal and circumferential) assessment of the ventricular myocardial deformation in these patients.

Keywords: Speckle Tracking Echocardiographic; Ventricular Functions; Pulmonary Hypertension; Shunt Disease

#### INTRODUCTION

Pulmonary hypertension (PH) is a progressive disease that carries high morbidity and mortality. Although cardiac catheterization is used to define PH, echocardiography is the most important non-invasive tool that is used to detect PH [1].

It provides the anatomy of the right heart, non-invasive hemodynamic assessment, systolic and diastolic evaluation of the right

heart, and serial follow-up for this patient population. A diagnostic classification has been developed and modified at the World Symposiums on Pulmonary Hypertension (WSPH). This clinical classification system identifies five categories of disorders that cause with each group sharing similar hemodynamic, pathologic, and management Pulmonary arterial features; hypertension (PAH) (Group 1); PH due to left heart disease

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(Group 2); PH due to chronic lung disease and/or hypoxia (Group 3); chronic thromboembolic PH (Group 4); and PH due to multifactorial mechanisms (Group 5)[2].

Pulmonary hypertension (PH) can be a rapidly progressive and fatal disease. Although right heart catheterization remains the gold standard in evaluation of PH, echocardiography remains an important tool in screening, diagnosing, evaluating, and following these patients [3,4].

Due to the special geometric features of the RV such as the tripartite morphology and different myofiber architecture, it sometimes be difficult to evaluate the RV by the standard techniques such as tricuspid annular plane systolic excursion (TAPSE) or RV myocardial performance index (RV MPI) [5].

So, the use of modern imaging techniques as speckle tracking echocardiography (STE) may be needed to sufficiently assess RV structures and functions. Recently, the new imaging modality speckle tracking echocardiography (STE) was proved to be similar to the cardiac magnetic resonance in reproducibility and accuracy [6].

Echocardiography is a valuable non-invasive tool in screening, diagnosing, and assessing pediatric PH. Echocardiography provides indirect measurements of pulmonary artery pressures, which can help in the initial assessment and follow-up of these patients. It also plays an important role in assessing outcomes, monitoring the efficacy of specific therapeutic interventions for PH, and detecting the preclinical stages of disease[7].

Speckle tracking Echocardiographic imaging is a relatively new echocardiographic modality that provides quantitative information about myocardial motion with high temporal and spatial resolution. STE may detect this impairment at a stage when conventional Echocardiographic indices are still normal. And so the use of STE is superior to that of conventional gray-scale [8].

# AIM OF THE WORK

The aim of this study was to assess the right and left ventricular functions and their strain pattern among Infants with pulmonary hypertension associated with shunt disease by 2-D speckle tracking echocardiography and correlate these finding with haemoynamic, clinical and Echocardiographic findings among such patients

## **PATIENTS AND METHODS**

This study was carried out on 44 patients at the Pediatric Cardiology Unit, Pediatric Department, Zagazig University Hospital, during the period from June 2018 to February 2019.

Written informed consent was obtained from all participants' parents and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

The patients were classified into 2 groups:

Group (I): Twenty-two patients were diagnosed as pulmonary hypertension associated with congenital intracardiac shunt disease.

Group (II): Twenty-two apparently healthy subjected were used as a control group.

#### Inclusion criteria:

- **1. Age:** one month to two years.
- **2.** Sex: both sexes are included
- 3. Infants presented with clinical and echocardiographic evidence of pulmonary hypertension and have normal LV systolic function measured using the biplane method of disks (modified Simpson's rule) according to Schiller [9].
- 4. Patients with left to right or right to left shunts, along with congenital heart diseases and pulmonary arterial hypertension.

### **Exclusion criteria:**

- inability to obtain adequate 2D image quality.
- Infants suffer from left heart diseases that may affect RV geometrical morphology.
- primary pulmonary hypertension, familial pulmonary hypertension, and evidence of any chronic systemic disease or pulmonary disease.
- Arrhythmia which may affect the image analysis.

All Cases and control were subjected to

- detailed history taking (age, sex, birth weight and duration of illness), Symptoms of pulmonary hypertension (cough, dyspnea, recurrent chest infection, hemoptysis, chest wheeze ......), Anti-failure drugs received (number, types, doses and duration), patient receiving angiotensin converting enzyme (Capotril) and Furosemide. Spironolactone is added to some patient with severe heart failure.
- clinical assessment, conventional echocardiographic examination and strain analysis based on combined speckle tracking algorithms applied on high-frequency ultrasound images

# Statistical analysis

Data were collected, tabulated and analyzed by SPSS 20, software for Windows. The significance level was set at P < 0.05.

## **RESULTS**

Table (1) showed that there was no statistical significant difference between the studied groups regarding age and sex. (P >0.05). Table (2) showed that there was statistical significant differences between cases and control as regarding Pulmonary artery pressure, weight, BMI, their vital signs and O<sub>2</sub> saturation. Table (3) showed that there was statistical significant difference between cases and control group as regarding longitudinal axes strain by speckle tracking of two dimension gray scale echo image finding at MID, Basal Post, Apical Anterior Sep and Basal Anterior sep. Table (4), showed that

there was statistical significant difference between cases and controls groups as regard circumferential axes of left ventricle by speckle tracking of two dimension gray scale echo image finding at all parameters (p<0.05) except Circum Bas Postoperatively (p>0.05). **Table** (5) showed that patients with pulmonary hypertension had significantly higher Right ventricle end diastolic diameter, ventricular free wall thickness and statistically **TAPSE** than controls. (P<0.001)respectively. Table (6) shows the speckletracking parameters of control group and PAH patients. RV free wall strain were significantly lower in PAH patients than in controls. RV free wall strain were higher in basal segment  $(-1.61\pm0.19)$  in comparison with the apical segment  $(-1.21\pm0.18)$  in healthy children, suggesting a base-to-apex gradient. This baseto-apex gradient was not observed in PAH children. However, in PAH patients there was a more expressed decrease of mean longitudinal strain in the basal region of the RV free wall compared with the apical one. Figure (1) demonstrated the AUROC(area under ROC) was 0.75.Optimum cut-off Pulmonary artery pressure (35.5mmHg)to predict LV global Longitudinal Average strain with Sensitivity 100%, specificity is 63% and accuracy is 77.3. This indicate that Pulmonary artery pressure good diagnostic test to detect LV global (Longitudinal Average) strain

Table (1):Distribution of studied groups regarding age and sex

Items	Studie			
	Cases No=22 Control No=22		(t)	
				p
Age (Month)	8.3±7.7	9.04±5.6	0.38	0.7(NS)
$\overline{X} \pm SD$	(1-24)	(2-15)		
(min-max)				
Sex no(%)	12(54.5)	8(36.4)	chi square	0.22(NS)
Female	10(45.5)	14(63.6)	=1.4	
Male	, , ,	, , ,		

(t) student t test of significant

**NS**= insignificant

Table (2): Mean± standard deviation of Pulmonary artery pressure, some anthropometric measurements and vital signs among studied cases in comparison to control:

, and the second	Studied groups			
	Cases	control	(t)	P
Pulmonary artery pressure (mmHg) $\overline{X} \pm SD$	53.2±5 (45-62)	34.2±1.2 (33-36)	17.2	0.0001(HS)
(min-max)				
Weight(kg)  X ±SD  (min-max)	5.9±2.6 (2-10.15)	7.6±2.5 (4.8-11.5)	MW	0. <b>03</b> (S)
Length(cm) $\overline{X} \pm SD$ (min-max)	68±16.3 (41-87)	69.9±14 (53-86)	0.4	0.68(NS)
BMI (kg/m <sup>2</sup> ) $\overline{X} \pm SD$ (min-max)	13±4.8 (4.62-25.51)	15.6±2.2 (12.17- 17.53)	MW	0.029(S)
Systolic Blood Pressure(mmHg)  X ±SD  (min-max)	96.5±11.1 (70-110)	90.9±3.5 (86-95)	2.3	0.03(S)
Diastolic Blood Pressure(mmHg)  X ±SD (min-max)	60.1±11.9 (40-80)	48.6±5.2 (40-55)	4	0.0001(HS)
Heart rate (beat/min) $\overline{X} \pm SD$ (min-max)	118.8±8.7 (108-139)	107.5±4.02 (102-112)	5.5	0.0001(HS)
iratory Rate (cycle/min) $\overline{X} \pm SD$ (min-max)	41.4±7.5 (36-72)	29.9±1.2 (28-31)	7.1	0.0001(HS)
O2_saturation(%)  X ±SD (min-max)	96.1±1.5 (92-98)	97.8±0.8 (97-99)	4.6	0.0001(HS)

MW = Mann Whitnney test S=significant <0.05 HS= highly significant p<0.001

Table (3): Comparison between studied groups as regard Left ventricle longitudinal axes strain

velocities by speckle tracking of two dimension gray scale ECHO.

Parameters Parameters Parameters	Studied gr	Test of significant	P	
	Cases	Control	significant	
BAS_Post (cm/sec)	4.1±1.8	2.7±0.9	(t)3.2	0.002(S)
$\overline{X} \pm SD$	(1.58-6.71)	(1.10-3.48)		
(min-max)				
MID_Post(cm/sec)	2.2±0.7	2.8±0.4	(t)3.5	<b>0.001(S)</b>
X ±SD	(0.80-3.69)	(2.30-3.31)		
(min-max)				
Apic_Lateral(cm/sec)	1.4±0.6	1.2±0.1	MW	0.358
X ±SD	(0.48-3.22)	(1.10-1.41)		
(min-max)				
Apic_Anter_Sep(cm/sec)	2.7±1.5	2.9±0.5	MW	0. <b>041</b> (S)
X ±SD	(0.93-7.10)	(2.30-3.51)		
(min-max)				
Mid_ANT_SEP(cm/sec)	3.7±2.2	2.7±0.7	MW	0.3(NS)
X ±SD	(1.51-8.60)	(2.03-3.54)		
(min-max)				
BAS_ANT_SEP(cm/sec)	4.4±2.5	4.8±0.4	MW	.038(S)
X ±SD	(1.59-9.10)	(4.40-5.20)		
(min-max)				
Average Global LV	3.1±1.2	2.7±0.2	MW	0.61(NS)
strain —	(1.64-5.20)	(2.45-2.89)		
X ±SD				
(min-max)				

MW=Mann-Whitnney u test

Table (4): Comparison between studied groups regard circumferential axes of left ventricular

strain% by speckle tracking of two dimension gray scale echo image:

parameters	Studie	Test of sig	p	
	Cases	control		
Circum_BAS_Ant_Sep strain% X ±SD (min-max)	-61.6±59.2 (-210.15:-17.14)	-58.4±5.01 (-65.10 :-50.17)	MW	0. <b>0001</b> (HS)
Circum_BAS_ANTstrain%  X ±SD (min-max)	-59.9±31.9 (-118.43 :-19.57)	-54.8±6.3 (-63.2:-45.73)	MW	0.45(NS)
$\begin{array}{l} \textbf{Circum\_Bas\_Lateralstrain\%} \\ \overline{X} \pm SD \\ (min\text{-}max) \end{array}$	-71.2±28.2 (-116.42 :-25.41)	-21.7±2.6 (-25.39:-18.25)	MW	0. <b>0001</b> (HS)
Circum_Bas_Post strain % X ±SD (min-max)	-58.7±24.7 (-112.74:-35.8))	-57.3±6.4 (-63.85:-45.5)	MW	0.13(NS)
Circum_Bas_Infstrain%  X ±SD (min-max)	-50.4±33.9 (-113.38 :-13.91)	-48.4±3.3 (-53.28 :-45.05)	MW	0.038(S)
Circum_Bas_Sepstrain%  X ±SD (min-max)	-68.7±42.6 (-179.85:-26.7)	-24.8±3 (-29.06 :-20.1)	MW	0.0001(HS)
Circum_Averagestrain%  X ±SD (min-max)	-60.2±27.6 (-112.16 :-31.02)	-44±3.8 (-49.47:-39.2)	MW	0.01(S)

MW=Mann-Whitnney u test

Table (5) Standard two-dimensional and M-mode parameters of right ventricle among studied cases in comparison to controls.

Parameters	Studied		P	
	Cases	control	(t)	
RVED (cm)  X ±SD (min-max)	$2.4 \pm 0.5$ (2.3- 2.6)	$1.2 \pm 0.4$ $(1.1 - 1.4)$	4.9	0.0001(HS)
$\frac{\text{RVT(cm)}}{\overline{X}}_{\pm \text{SD}}$ (min-max)	0.8 ±0.2 (0.6-0.9)	$0.3 \pm 0.1$ $(0.2-0.5)$	5.2	0.0001(HS)
$\frac{\text{TAPSE mm}}{X}_{\pm \text{SD}}$ (min-max)	$15 \pm 1.3$ (13.1- 17.2)	$19.7 \pm 2.4$ (17.4- 21.2)	4.221	0.0001(HS)

RVED-parasternal long axis view right ventricle end diastolic diameter; RVT-right ventricle free wall thickness; - TAPSE - tricuspid annular plane systolic excursion

Table (6):Comparison between studied groups as regard right ventricle free wall longitudinal axes strain velocities by speckle tracking of two dimension gray scale echo image

	Cases	Control	Test of significant	P
Basal RV free wall (cm/sec)  X ±SD (min-max)	-12.86 ± 4.5 (-10.114.6)	-26.61 ± 3.19 (-23.828.2)	20.20	0.0001(HS)
Mid RV free wall (cm/sec) $\overline{X} \pm SD$ (min-max)	$-17.2 \pm 5.31$ (-15.318.3)	$-24.50 \pm 4.17$ (-20.333.1)	10.754	0.0001(HS)
Apical RV free (cm/sec) wall(cm/sec) X ±SD (min-max)	-16.04 ± 4.16 (-12.420.5)	-20.21 ± 7.18 (-19.228.6)	2.748	0.05 (S)
Average RVGLS (cm/sec) X ±SD (min-max)	$-15.6 \pm 3.5$ (-12.416.2)	-22.4 ± 7.09 (-19.835.9)	MW 8.813	0.001(HS)

MW=Mann-Whitnney u test

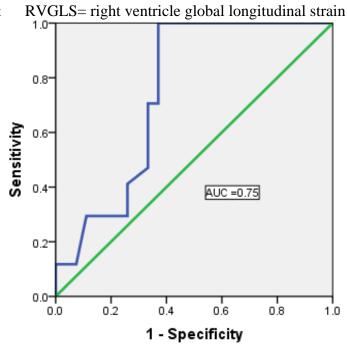


Figure (1): ROC curve of for the validity of Pulmonary artery pressure systolic to predict LV global (Longitudinal Average) strain

### **DISCUSSION**

In the current study, the range for age of pulmonary hypertension associated congenital intracardiac shunt disease patients were 1-24 months with the mean 8.3±7.7, the male represented about (45.5%) of patients and the females represented about (54.5%) of patients. Patients and controls were properly matched regarding age and sex. There were no statistically significant difference between cases and control as regarding age and sex (p>0.05), these results were in agreement with Yıldız et al. [10] who found that the demographic study showed non-significant difference between with congenital heart patients diseases associated with pulmonary arterial hypertension and control.

In the present study, the mean of weight was 5.9±2.6 Kg in cases while it was 7.6±2.5 Kg in control group with statistically significant difference (p value < 0.05). This was in agreement with **Muntean et al., [11]** who found that there was a statistically significant difference between patient and control group as regard weight. This can be probably explained by the impact of disease on nutritional status of PAH patients.

In the present study, the mean length was 68±16.3 Cm among cases while it was 69.9±14 Cm among control group with no statistically significant difference (p value>0.05). This was in agreement with **Muntean et al., [11]** who found that there was no statistically significant difference between patient and control group as regard length.

In the present study, the mean of BMI was 13±4.8 in cases while it was 15.6±2.2 in control group with a statistically significant difference (p value < 0.05). This was in agreement with **Muntean et al., [11]** who found that there was a statistically significant difference between patient and control group as regard BMI. This can be probably explained by the impact of disease on nutritional status of PAH patients and in disagreement with this study, **Sanli et al. [12]** found that there was no significant difference among groups as regard body mass index.

In the present study the values of Systolic and diastolic blood pressure showed a statistically significant difference between control & patient with PAH. This goes in contrast with a study done by Yıldız et al. [10] where there was no significant difference between systolic and diastolic blood pressure in different groups. But it was a study applied in adults.

In the present study, the mean of  $O_2$  saturation% was  $96.1\pm1.5$  in cases while it was  $97.8\pm0.8$  in control group with highly statistically significant difference (p value < 0.0001). This was in agreement with **Muntean et al., [11]** who found that there was highly statistically significant difference between patient and control group as regard  $O_2$  saturation, and also the study of **Cua et al.[13]** who showed that there was a significant difference in PH patients versus control group in oxygen saturation.

In the present study pulmonary arterial pressure measured by Echocardiography of cases ranged from 45 to 62 with the mean  $53.2\pm5$  while pulmonary arterial pressure of control ranged from 33 to 36 with the mean  $34.2\pm1.2$  with highly statistically significant difference between them (p value < 0.0001). In agreement with this study, **Ramani et al., [14]** found that the mean pulmonary artery pressure was  $62\pm20$  mmHg, ranged from 41 mmHg to 95 mmHg in case group.

Assessment of left ventricular systolic and diastolic functions in our study by echocardiographic conventional methods showed a statistically non significant differences between cases and controls This came in agreement with **Güvenc et al. [15]**.

Our results showed that, the mean of circumferential basal septal circumferential average, circumferential stander deviation  $-68.7\pm42.6$ ,  $-60.2\pm27.6$ was 24.5±10.9 respectively in cases while it was - $24.8\pm3$ ,  $-44\pm3.8$ ,  $16.3\pm1.3$  respectively in control group with statistically high significant differences between the two groups. nd to summarize that the circumferential basal :lateral, septal and anterior strains are significantly higher among cases than controls (P<0.001).

Muntean et al., [11] found that the mean of circumferential basal anterior, the mean of circumferential basal lateral, the mean of circumferential basal inferior in adults was higher among cases than among control group with statistically significant difference between the groups.

We have found that, the mean longitudinal strain of basal posterior, mid posterior, apical anterior septum, basal anterior septum was  $4.1\pm1.8$ ,  $2.2\pm0.7$ ,  $2.7\pm1.5$ ,  $4.4\pm2.5$  respectively in cases while it was  $2.7\pm0.9$ ,  $2.8\pm0.4$ ,  $2.9\pm0.5$ ,  $4.8\pm0.4$  respectively in control group with statistically significant difference between the groups. In agreement with this study, **Ramani et al.**, [14] found that there was a statistically significant difference between the groups regarding the mean of basal posterior, basal anterior, basal anterior septal (p value <0.05) except apical anterior septum (p value >0.05).

In the present study, the mean of LV longitudinal apical lateral, mid anterior septum was  $1.4\pm0.6$ ,  $3.7\pm2.2$  respectively in cases while it was  $1.2\pm0.1$ ,  $2.7\pm0.7$  respectively in control group with no statistically significant difference between the groups. In agreement with this study, **Ramani et al.**, [14] found that there was no statistically significant difference between the groups regarding the mean of apical lateral.

Furthermore, we found a significant negative correlation of Mid and Apical RV free wall strain indices with the degree of Pulmonary artery pressure. Mauritz et al [16], reported that in RV the longitudinal shortening reduction starts at the basal level and continue to decrease in other regions until a lower limit is reached. Also, they suggested that a further reduction of RV function is due to loss of transverse shortening with leftward septal displacement.

In our study, we demonstrated ventricular interdependence by identifying impairment in LV contractility, correlating reduction in longitudinal systolic strain of the

LV free wall with a reduction in longitudinal systolic strain in the RV free wall in patients with PAH. We also showed that while conventional measures of LV systolic function remained normal, LV systolic strain was significantly reduced in concert with reduced RV systolic strain.

Macroscopic fiber direction studies have demonstrated a continuum of the subepicardial RV muscle plane along the posterior LV to the region of the left fibrous trigone. Oh et al., [17] has shown that these fibers descend from the left fibrous trigone to the LV apex (descending segment).

Conclusions: Two-dimensional speckle-tracking echocardiography is a complementary non-invasive tool for assessment of right and left ventricular function in children with pulmonary arterial hypertension, allowing analysis of both segmental and global (longitudinal and circumferential) assessment of the ventricular myocardial deformation in these patients.

#### **Declaration of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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