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# Speckle tracking of left ventricle in pediatric patients with hemodynamically significant patent ductus arteriosus (PDA): case–control study

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## Abstract

**Background** Left ventricle (LV) volume overload is observed with hemodynamically significant PDA as it causes left to right shunting, leading to increased pulmonary blood flow. This overload causes LV remodeling as LV increases stroke volume in trial for compensation, but in larger shunts, patients may develop symptoms of congestive heart failure. Two-dimensional (2D) speckle-tracking echocardiography has emerged as a technique for objective and quantitative evaluation of global and regional myocardial function, independent of the angle of myocardial insonation.

**Aim of the work** This study aimed to evaluate left ventricular function by 2-dimensional speckle tracking in children with hemodynamically significant PDA.

**Methods** This prospective controlled study was performed on 54 children divided into two groups (34 as cases and 20 as controls) to compare echocardiographic measurements. Conventional Echocardiography, tissue Doppler, and Speckle tracking were done for all patients, and measurements were compared.

**Results** There was a statistically significant difference ( $p$  value  $< 0.001$ ) in global longitudinal strain (GLS) in the PDA group indicating a decrease in LV function in PDA patients. This difference was observed in several conventional echocardiographic parameters but not in tissue Doppler in our study.

**Conclusion** Left ventricle global strain is an important predictor of the myocardial performance index of the Left ventricle in patients with hemodynamically significant PDA and outweighs other conventional echocardiographic parameters and tissue Doppler indices.

**Keywords** GLS, Echocardiography, PDA

## Background

Left ventricle (LV) volume overload is observed with hemodynamically significant PDA as it results in the shunting of blood from the left ventricle to the right ventricle increasing pulmonary blood flow. This overload causes LV remodeling as LV increases stroke volume in trial for compensation, but in larger shunts, patients may develop symptoms of congestive heart failure [1].

The hemodynamic effects of PDA differ between different patients. The pulmonary vascular resistance drops significantly at birth, so a continuous left-to-right shunt

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develops if an infant suffers from PDA. According to the Poiseuille Law, this shunt has a positive relationship to the pressure gradient between the aorta and pulmonary artery and a negative relationship to the resistance to flow. The pulmonary and systemic resistances change significantly in patients with large PDA while this is not observed in smaller ones due to high resistance. There are adjustable factors that affect pulmonary vascular resistance like oxygen tension and blood PH which affect trans-ducial flow [2].

A left-to-right shunt from PDA results in increased pulmonary blood flow. The level of this shunt and its connected cardiopulmonary effect determines the pathophysiologic characteristics of this lesion in clinical care. Special hemodynamic characteristics associated with premature neonates make them more vulnerable to PDA-associated cardiorespiratory compromise. PDA left to right flow causes increased pulmonary blood flow and dilatation of the left heart. This results in increased left ventricular end-diastolic pressures, which elevates pulmonary venous pressure, and pulmonary congestion. This effect is well observed in preterm neonates because of the greater adaptability of their immature ventricles [3].

Two-dimensional (2D) speckle tracking is a new echocardiography technique developed for functional and quantitative assessment of myocardium globally and regionally regardless of myocardial insonation angle [4].

The main advantage of this new technique is not just it assesses the global myocardial function, but also that it detects any changes in regional myocardial deformation changes that cannot be visualized using the usual 2D parameters [5].

### Aim of work

The aim of this study was to evaluate left ventricular function by 2-dimensional speckle tracking in children with hemodynamically significant PDA.

### Methods

This study is a prospective analytical case–control study on 34 infants and children. This study was conducted at a tertiary care university hospital from November 2022 to January 2024, with audible PDA.

A control group consisting of 20 healthy infants and children was included in the study for comparison of echocardiographic measurements.

### Inclusion criteria

Patients in pediatric age ranging from 6 months to 18 years whose weight is over 6 kg with audible PDA with or without evidence of LV volume overload were included in the study.

### Exclusion criteria

- Patients with PDA not eligible for transcatheter closure
- Patients with PDA suffer from other significant congenital heart diseases or irreversible pulmonary vascular diseases.

### Patients evaluation

All Participants were evaluated as follows: complete history taking, full examination with special emphasis on anthropometric measurements, and local examination with detailed cardiac examination.

### Investigations

All children were submitted to routine investigations, chest X-ray, ECG, and detailed transthoracic echocardiography (TTE) using different modes including 2D TTE, tissue Doppler imaging (TDI), and 2D STE.

A- Routine echocardiographic examination

B- Examination using tissue Doppler.

C- Speckling tracking imaging 2D echocardiography

### Equipment

- Machine: echocardiographic evaluation was done using a commercially available ultrasound transducer and equipment (Vivid E95, GE Healthcare, Horten, Norway).
- Transducers: data acquisition was performed with a 3.5-MHz transducer, S7 probe. Workstation: Digital loops were obtained and analyzed using AFI software on the Equipment.

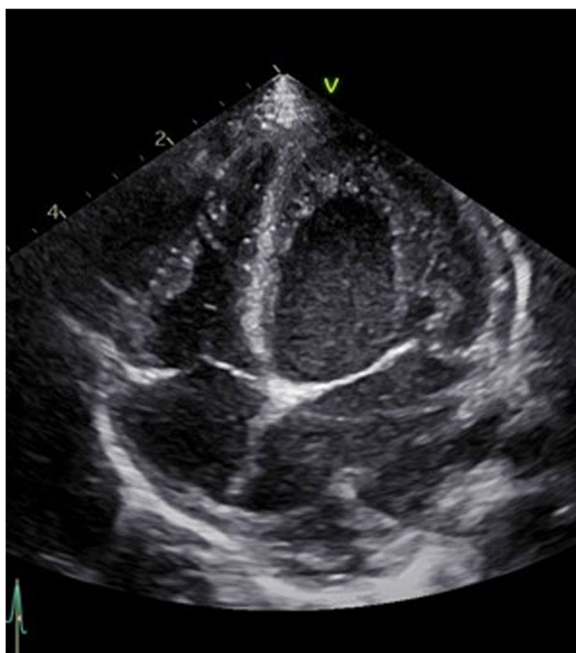
#### A) Routine echocardiographic examination

The study was done for all participants (cases and controls) using the standard views (apical, parasternal long axis, parasternal short axis, and subcostal) to gather all data required for comparison according to the American Society of Echocardiography guidelines (Figs. 1, 2, 3, and 4) [6].

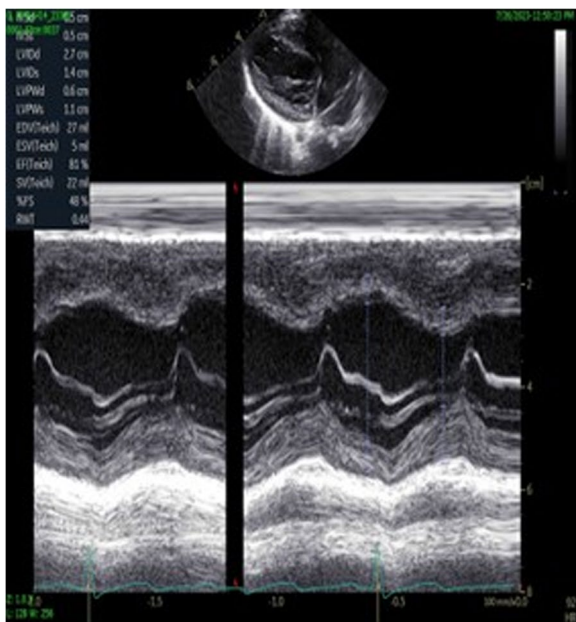
#### B) Examination using tissue Doppler (TDE)

- Mitral annulus velocities:

PW-TDI sample volume is positioned at the septal mitral annulus producing three waves, an antegrade systolic wave  $S'$  and two retrograde waves,  $E'$  repre-



**Fig. 1** Apical 4 chamber view of 7-month-old patient with PDA

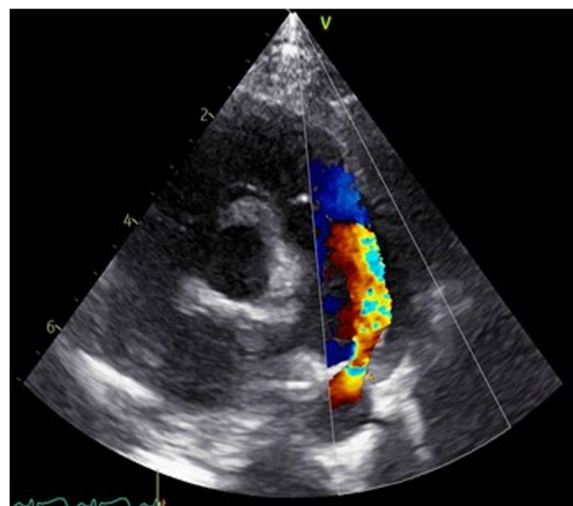


**Fig. 2** M mode from PLAX view of 7-month-old patient

senting passive LV filling and A' wave representing atrial contraction.

- Myocardial performance index of left ventricle (MPI):

The MPI was calculated using the Tei index which equals the difference between a' and b' divided by b'. a'



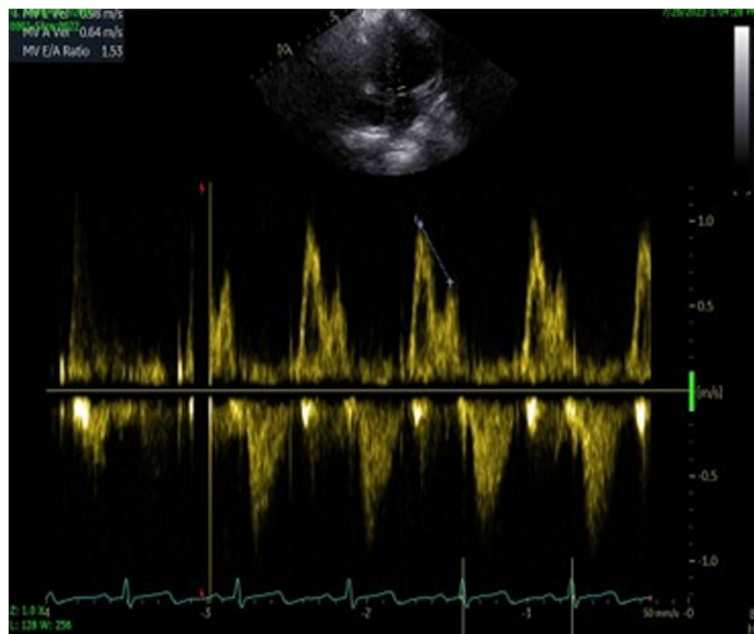
**Fig. 3** Modified parasternal short axis view showing Hemodynamically significant PDA in 1-year-old patient measuring 3 mm at the pulmonary end

is the time from the end of the A'-wave to the beginning of the E'-wave and b' is the time duration of the S' wave (Fig. 5).

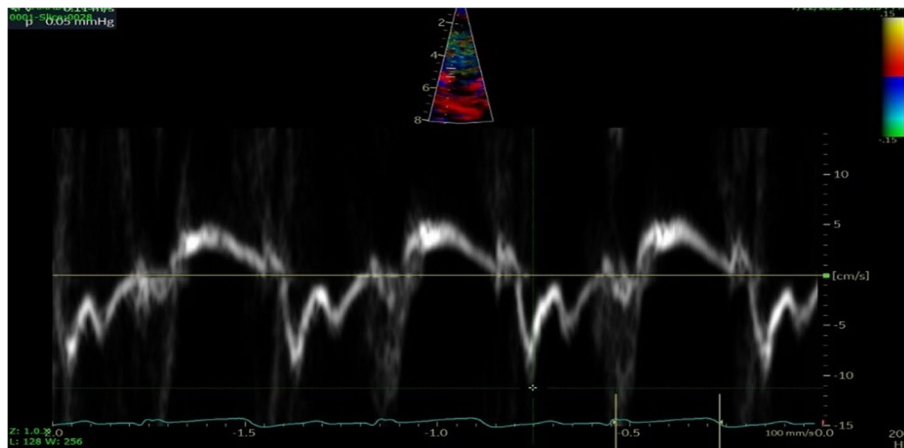
**C) Speckling tracking imaging transthoracic 2D echocardiographic examination**

A 3.5-MHz transducer, S7 probe interfaced with a GE Vivid E95 ultrasound system was used to image each heart. We used the 2D LVQ AFI function of the device to assess global longitudinal, circumferential, and radial strain and area strain. Three views were obtained 4 chambers, 2 chambers, and APLAX (Figs. 6, 7, and 8 respectively).

The speckle tracking of the left ventricle was done beginning from a region of interest (ROI) defined at the end of the systole. 2D strain analysis was performed at the end of the process in the 2D auto left ventricular auto quantification tool, which also calculated the volume and mass of the left ventricle. The meshes obtained from the two measurements were used for the 2D ROI strain. The 2D ROI strain was generated in an automatic manner using the end-systolic frame and was generated from an endocardial and an epicardial mesh (Fig. 9). The mesh of the endocardium was dependent on the one used for the measurement of end-systolic volume (ESV). The mesh of epicardium was produced automatically from the epicardial mesh used in the stage of left ventricle mass, by generating it from the end of diastole to the end of systole. The operator can adjust the shape of ROI by putting drawer points to pull the nearby ROI border towards where the operator wants it to go from the results of tracking, several parameters result from 2D



**Fig. 4** PW-Doppler in PDA patient showing EA ratio 1.53



**Fig. 5** Tissue Doppler of 1.5-year-old patient with PDA, TEI index 0.62

strain, including longitudinal, circumferential, area, and radial strain.

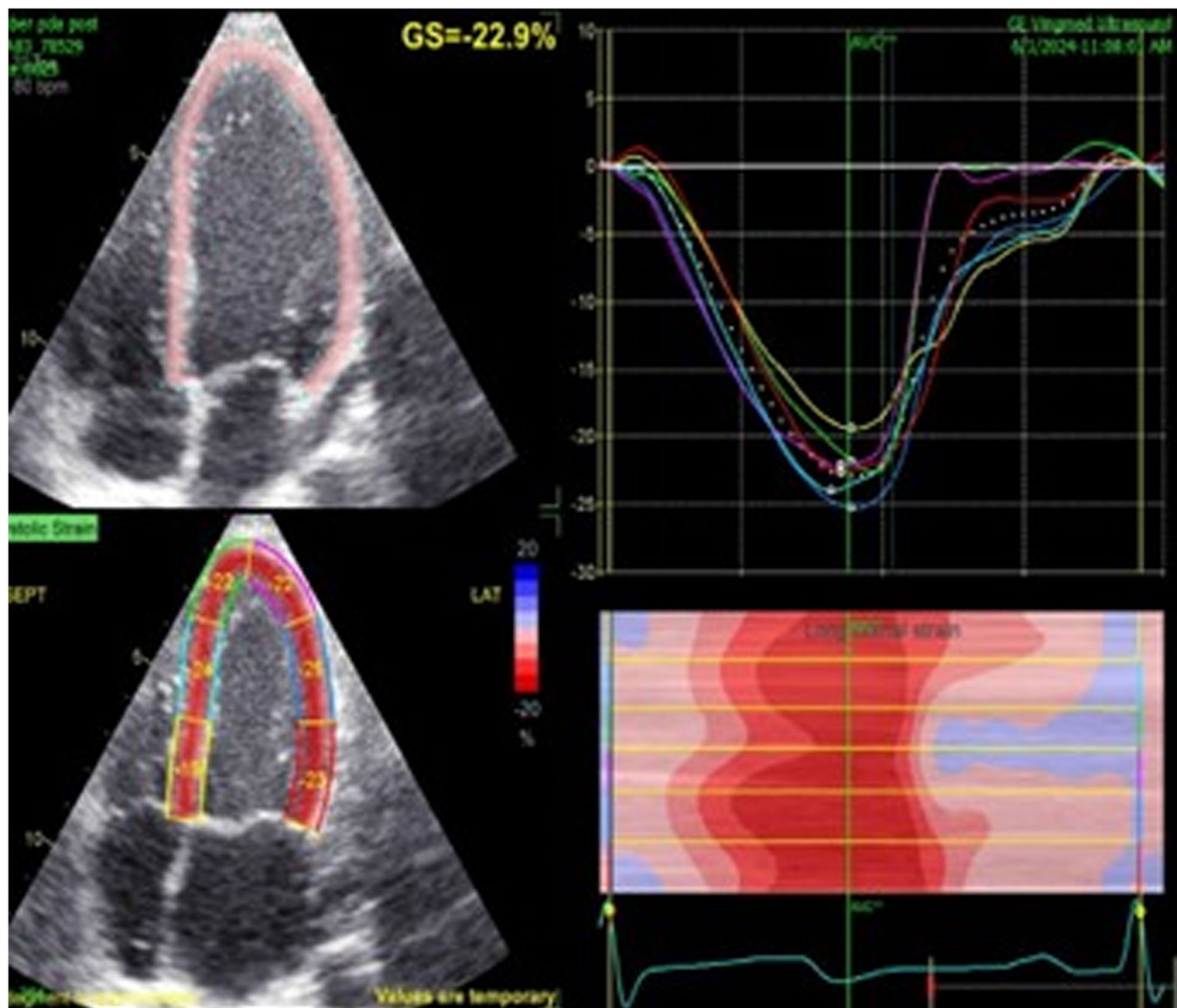
#### Assessment of variability

For the assessment of intra-observer variability, the same operator twice measured the analysis of the 2D strain of 15 participants who were selected randomly at an interval of 2 months to avoid recall bias. For interobserver variability assessment, the measurements of 2D strain were operated by a second observer who was not informed of the results of the first operator.

#### Statistical analysis and data interpretation

SPSS software, version 25 (SPSS Inc., PASW statistics for Windows version 25. Chicago: SPSS Inc.) was used for the analysis of data. Number and percent described qualitative data. Median (minimum and maximum) used in quantitative data for non-normally distributed data and mean (Standard deviation) for normally distributed data after using the Kolmogrov-Smirnov test or testing normality.

The judgment of the result's significance was at the ( $\leq 0.05$ ) level.



**Fig. 6** 4-chamber view for AFI LV strain calculation

- We used chi-square, Monte Carlo tests, and Fisher exact test for qualitative data comparison between groups.
- We used the Mann–Whitney  $U$  test for comparison between 2 studied groups for non-normally distributed data.
- We used the Student  $t$ -test for comparison of the 2 independent groups for normally distributed data.
- We used the Wilcoxon signed rank test for comparison between 2 studied periods for non-normally distributed data.

## Results

Regarding demographic data, there was a statistical difference regarding weight and BSA in the PDA group with a  $p$  value  $<0.001^*$  as illustrated in Table 1.

Regarding clinical presentation of PDA cases, the most common complaint was repeated chest infection in 27 cases (80%). Four cases were asymptomatic and discovered incidentally by PDA murmur auscultation in routine clinical examination as illustrated in Fig. 10.

LVIDD in PDA cases was statistically significantly higher than in the control group, with  $z$  score  $p$  value less than 0.001 as illustrated in Table 2 and Fig. 11.

Some of the conventional echocardiographic M mode indices were significant and indicated dilated left ventricle-like interventricular septum thickness in diastole (IVSd) and in systole (IVSs), the posterior wall thickness in systole of the left ventricle (LVPWs) and Stroke volume (SV) as indicated in Table 3 and Fig. 12. LA/AO ratio is statistically significant between 2 groups indicating LA dilation in PDA cases.

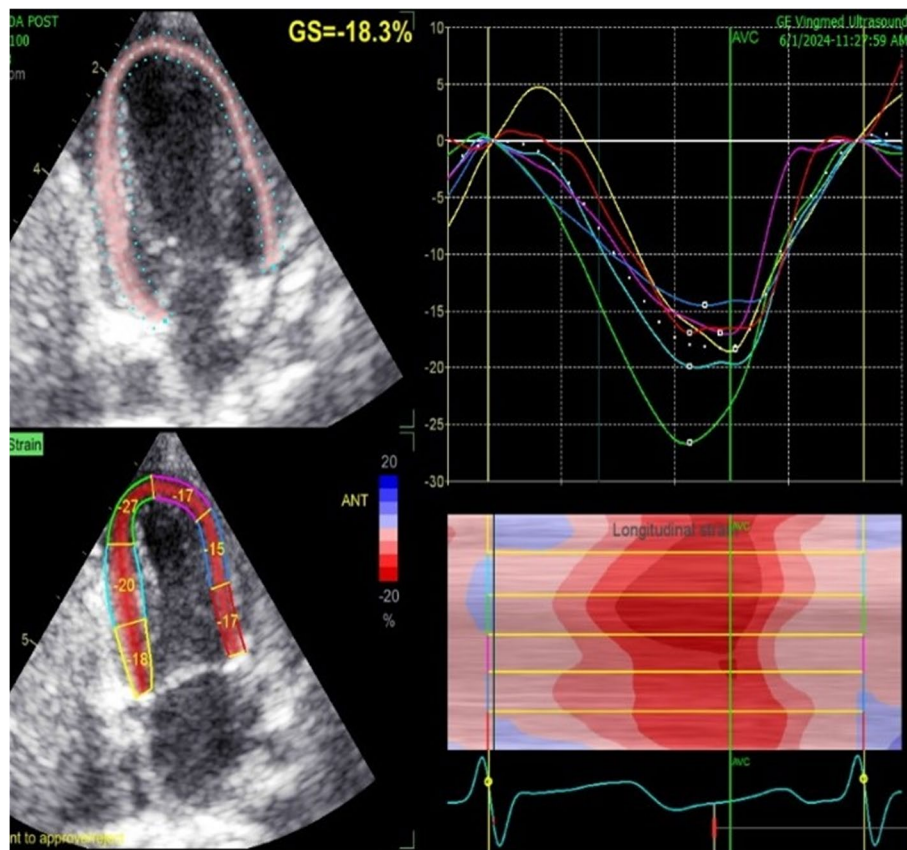


Fig. 7 2-chamber view for AFI LV strain calculation

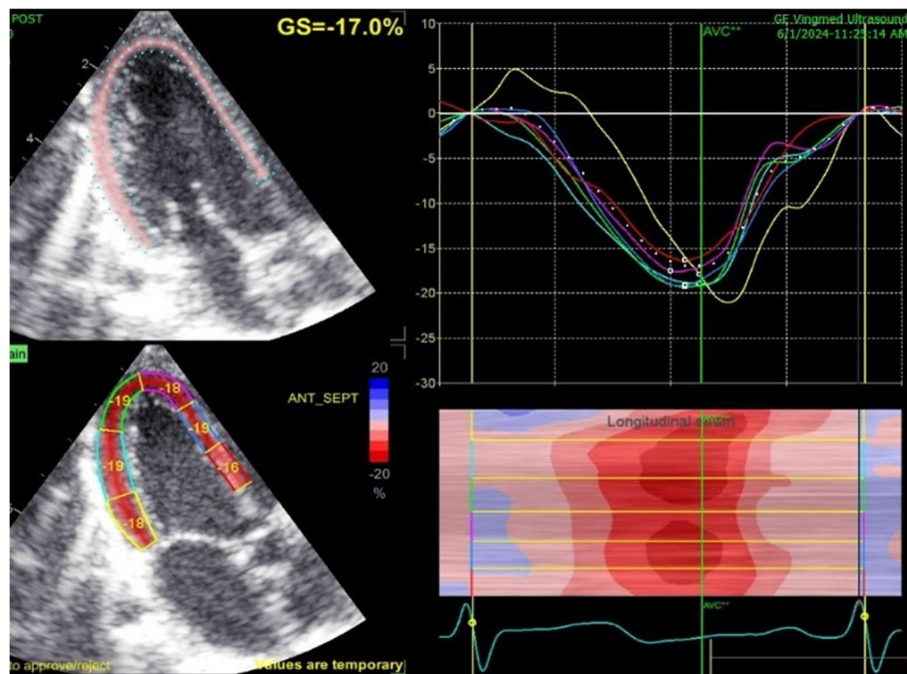
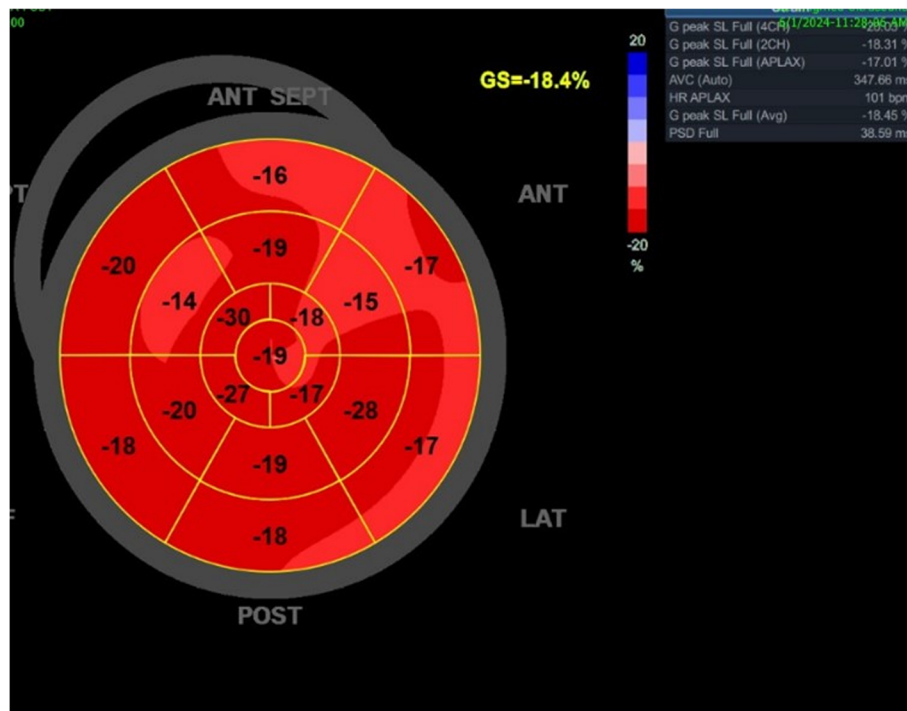


Fig. 8 3-chamber view for AFI LV strain calculation



**Fig. 9** Bull's eye of a 1.5-year-old patient with hemodynamically significant PDA. GS was 18.4%

**Table 1** Comparison of demographic characters between studied groups

	Cases group (n = 34)	Control group (n = 20)	Test of significance	p value
Age/years	2(0.5–14.0)	5.0(1.0–12.0)	Z = 1.87	0.062
Weight (kg)	10(6–43)	21(10–52)	Z = 3.80	<0.001*
Height (cm)	89(55–161)	131(80–155)	Z = 4.09	<0.001*
BMI (kg/m <sup>2</sup> )	15.29 ± 3.48	14.68 ± 4.63	t = 0.551	0.584
BSA	0.498(0.31–1.39)	0.90(0.49–1.47)	Z = 3.98	<0.001*

Data expressed as mean ± SD, median (min–max)

z Mann–Whitney U test, t Student's t test

\* Statistically significant

Pulsed wave Doppler showed increased E and A velocity across the mitral annulus while the E /A ratio was not statistically different as illustrated in Table 4.

Tissue Doppler findings in PDA cases show statistically significant increased A velocity while the Tei index was increased but not statistically significant as illustrated in Table 5.

Speckle tracking comparison showed that all global strain in all acquired views was statistically lower in the PDA group with p value < 0.05 except peak strain dispersion (PSD) which was lower but not statistically significant as illustrated in Table 6 and Figs. 13, 14 and 15.

### Discussion

Our study was performed to evaluate left ventricle function with 2-dimensional speckle tracking echocardiography and to evaluate if there is an advantage of speckle tracking over conventional echocardiography techniques and tissue Doppler in detecting changes in left ventricle systolic function.

Clinical data showed that the most presenting clinical manifestation to hospital or outpatient clinics in this PDA group was repeated chest infections (80%), poor weight gain (75%), dyspnea (60%), and difficulty in feeding (50%). This observation agrees with the clinical

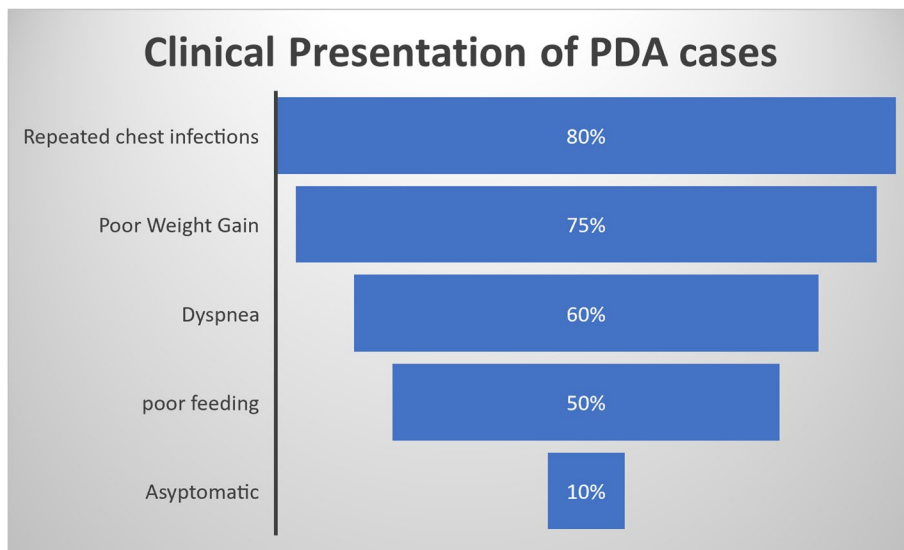


Fig. 10 Funnel chart of clinical presentation of PDA cases

Table 2 Comparison of LVIDD and z score pre-PDA closure between studied groups

	Cases group (n=34)	Control group (n=20)	z	p value
LVIDD	3.2(2.2–5.4)	3.43(2.3–4.33)	2.31	0.021*
z score	1.085 (–1.2, 10.06)	–1.1 (–1.9, 1.6)	4.37	<0.001*

LVIDd left ventricle internal diameter at end-diastole

Data expressed as median (min–max)

z Mann–Whitney U test

\* Statistically significant

Scenario of PDA children who commonly suffer from failure to thrive, difficulty in feeding, and dyspnea depending on the size of the PDA and quantity of left-to-right shunting [7].

In our study, the PDA patient’s median age was 2 years (ranging from 6 months to 14 years), This was matched with controls of close age to not affect the measured echocardiographic indices.

Demographic data revealed that the median weight of the PDA group was 10 kg (ranging from 6 to 43 kg),

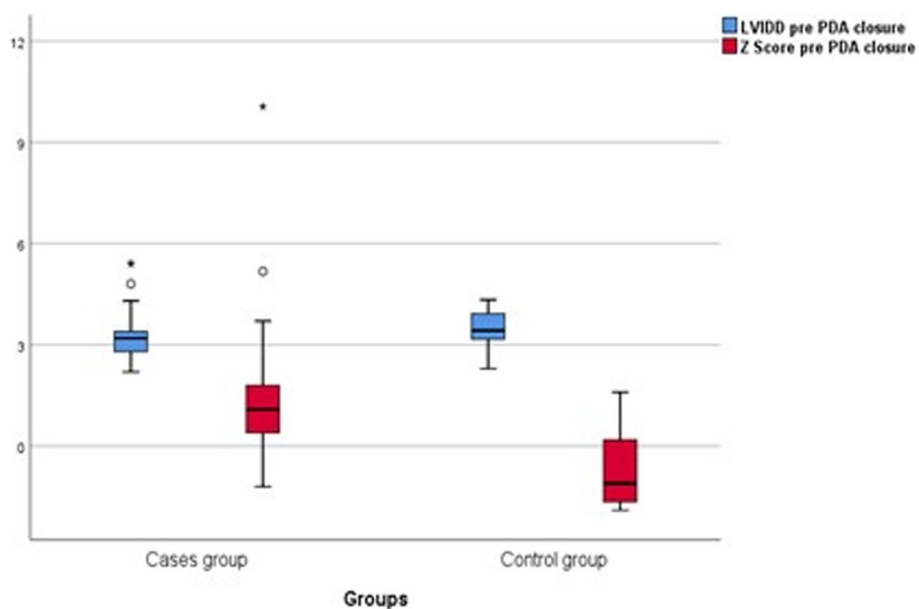


Fig. 11 Box and whisker plot of LVIDd and z score in PDA cases and control



**Table 3** Comparison of M-mode functions pre-PDA closure between studied groups

M-mode	Cases group (n = 34)	Control group (n = 20)	z	p value
IVSd (cm)	0.5(0.3–1.1)	0.735(0.46–1.1)	3.72	<0.001*
IVSs (cm)	0.80(0.5–1.4)	1.0(0.61–1.4)	2.75	0.006*
LVIDd (cm)	3.2(2.2–5.4)	3.43(2.3–4.33)	2.31	0.021*
LVIDs (cm)	2.0(1.4–3.5)	2.0(1.5–2.65)	0.541	0.589
LVPWd (cm)	0.60(0.3–0.90)	0.585(0.43–1.02)	0.353	0.724
LVPWs (cm)	0.9(0.3–1.5)	0.95(0.86–1.6)	2.69	0.007*
EDV (ml)	41(16–140)	48.5(17–84)	2.33	0.02*
ESV (ml)	13(5–50)	12.4(6–25.8)	0.539	0.590
FS (%)	37(29–49)	39(31–48)	0.977	0.328
SV (ml)	28(10–105)	35(12–57)	2.23	0.026*
EF (%)	66(57–82)	69(60–80)	1.67	0.095
RWT	0.39(0.23–0.54)	0.30(0.20–0.70)	1.31	0.190
LA (cm)	1.9(1.4–2.8)	1.8(1.3–2.3)	0.668	0.504
AO (cm)	1.1(0.8–3.0)	1.75(0.9–2.5)	0.67	0.64
LA/AO	1.5(0.9–2.1)	1.2(0.8–1.4)	4.44	<0.001*

Data expressed as median (min–max)

z Mann–Whitney U test

IVSd Interventricular septal thickness in diastole, IVSs Interventricular thickness in systole, LVIDd Left ventricular internal diameter at end systole, LVIDs Left ventricular internal diameter at end diastole, LVPWd Left ventricular posterior wall thickness in diastole, LVPWs Left ventricular posterior wall thickness in systole, EDV End-diastolic volume, ESV End systolic volume, FS Fractional shortening, SV Stroke volume, EF Ejection fraction, RWT Relative wall thickness, LA Left atrium diameter, AO Aortic root diameter

\* Statistically significant

BSA median was 0.49 (ranging from 0.31 to 1.39). These parameters were statistically significantly lower than the control group which illustrates the effect of PDA on the growth parameters of children, especially weight. This was reported in a study by Kunel et al. which studied premature infant that was managed by PDA surgical closure and observed flatter of their growth [8].

Conventional echocardiography M mode parameters illustrated that LVIDd was increased in the PDA group and by calculation of the z score, it was higher than the control group. Both parameters were statistically significantly higher. This is because of volume overload that occurs in hemodynamically significant PDA [9].

Also with conventional echocardiography M mode, IVSd, IVSs, and LVPWs were increased with statistical differences in the control group which indicates hypertrophy of the left ventricle due to volume overload of the heart. Also stroke volume was increased in the PDA group due to dilatation and hypertrophy of the Left ventricle according to Frank Sterling Law [10].

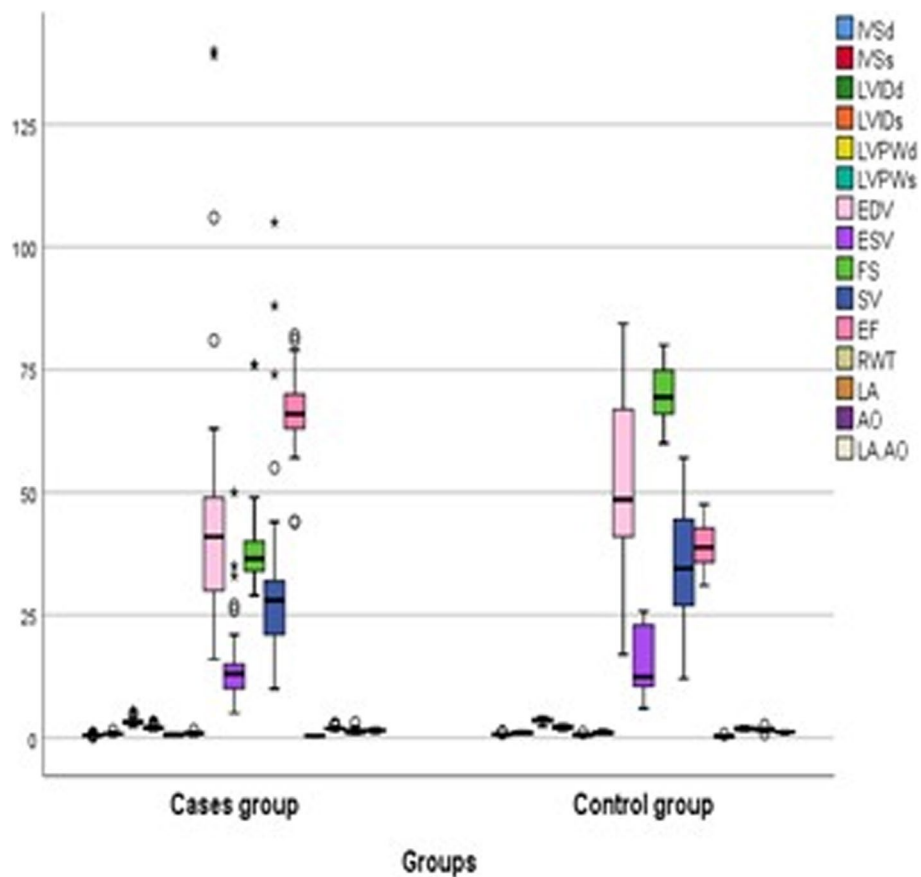
Regarding PW Doppler echocardiography A velocity and E velocity were statistically significantly higher in the PDA group in relation to the control group while

the E/A ratio was lower than that of the control but was not statistically significant. This increase in E velocity is mainly due to an increase in LA pressure due to diastolic dysfunction [11]. E/A ratio is within normal level due to increased E velocity as well as increased A velocity this represents grade 2 diastolic dysfunction [12].

Regarding the tissue Doppler, the Tei index was increased in the PDA group but not statistically different from the control. The Tei index evaluates the performance of the myocardium (MPI) and is used to detect combined ventricular systolic and diastolic function [13]. The MPI value has an inverse relationship to myocardial function; if MPI is increased, this indicates global myocardial function deterioration [14]. In a study by Zhou et al., the Tei index of children diagnosed with PDA was statistically significantly higher than that of the control group ( $p < 0.05$ ) [15]. The Tei index was higher but not statistically significant in our study. A/ velocity was statistically significantly increased due to increased atrial filling pressure during atrial contraction in late diastole because of impaired diastolic function of the left ventricle. The pressure of the left atrium is elevating with the reduction in left ventricular compliance [16].

Regarding speckle tracking of LV, all values of global strain in the 4-chamber and 2-chamber view and APLAX view were statistically significantly lower than comparing controls with  $p$  value  $< 0.001$ . we used the LV AFI method for the calculation of global strain after good acquisition of images in the views with automated results of Global strain and Bull's eye of LV strain which was also statistically significantly lower than comparing controls with  $p$  value  $< 0.001$ . The median average GS was  $-19.9$  (ranging from  $-16$  to  $-23$ ). Although these results are within normal values of LV strain, in comparison with controls, it indicates impaired systolic function of LV in the PDA group. This is compatible with other studies published in the literature which indicated that global longitudinal strain (GLS) of the left ventricle is a useful single predictor of MPI in PDA patients before and after PDA surgical or percutaneous closure [17].

Global longitudinal strain in our study and other studies is impaired in PDA patients indicating the effect of PDA on the left ventricle myocardial performance index. Unlike other echocardiography parameters like LVIDd which was elevated in our study but in other studies was not different from control [18]. While the E/A ratio was not impaired in our study, it was impaired in other studies [15]. Also, the tissue Doppler Tei index was not statistically different from controls in our study while in other studies it was statistically elevated in PDA patients like the study by Agha et al. [17]. This means that GLS could be the useful sole indicator of LV function in patients with hemodynamically significant PDA.



**Fig. 12** Box and whisker plot of M mode findings in PDA cases and control

**Table 4** Comparison of Pw Doppler pre-PDA closure between studied groups

PW-Doppler	Cases group (n = 34)	Control group (n = 20)	z	p value
E Vel(cm/s)	1.09(0.85–1.62)	0.87(0.7–1.1)	3.99	<0.0001*
A Vel(cm/s)	0.76(0.5–1.28)	0.565(0.43–0.85)	3.49	<0.001*
E/A	1.43(0.79–1.96)	1.5(1.2–1.8)	1.48	0.138

Data expressed as median (min–max)

z Mann–Whitney U test

E Vel/ Mitral valve velocity peak early velocity, A Vel/ Mitral valve peak late velocity

\* Statistically significant

**Limitations**

The number of PDA cases and healthy controls were relatively small. Another limitation was that our study didn't include neonates suffering from PDA, this was because of the study settings as we included the PDA cases who were planned for percutaneous PDA closure from the catheterization clinic in our hospital. Also, while performing 2DSTE there was difficulty in adjusting speckles on the region of interest by the current available software.

So, Software packages need to be adjusted to be suitable for children less than 20 kg.

**Conclusion**

Left ventricle global strain is an important predictor of the myocardial performance index of the left ventricle in patients with hemodynamically significant PDA and outweighs other conventional echocardiographic parameters and tissue Doppler indices.

**Table 5** Comparison of tissue Doppler pre-PDA closure between studied groups

Tissue Doppler	Cases group (n = 34)	Control group (n = 20)	z	p value
E'Vel (m/s)	0.115(0.07–0.21)	0.14(0.10–0.16)	1.70	0.089
A'Vel (m/s)	0.08(0.01–0.60)	0.07(0.05–0.10)	2.49	0.013*
S'Vel (m/s)	0.08(0.02–0.12)	0.065(0.05–0.90)	1.37	0.170
Tei index	0.520(0.37–1.7)	0.485(0.3–0.70)	1.51	0.132

Data expressed as median (min–max)

z Mann–Whitney U test

E'Vel Mitral valve septal leaflet early peak velocity in tissue Doppler, A'Vel mitral valve septal leaflet late peak velocity in tissue Doppler mode, Tei index myocardial performance index and S'Vel Mitral valve septal leaflet peak systolic velocity

\* Statistically significant

**Table 6** Comparison of speckle tracking of left ventricle pre-PDA closure between studied groups

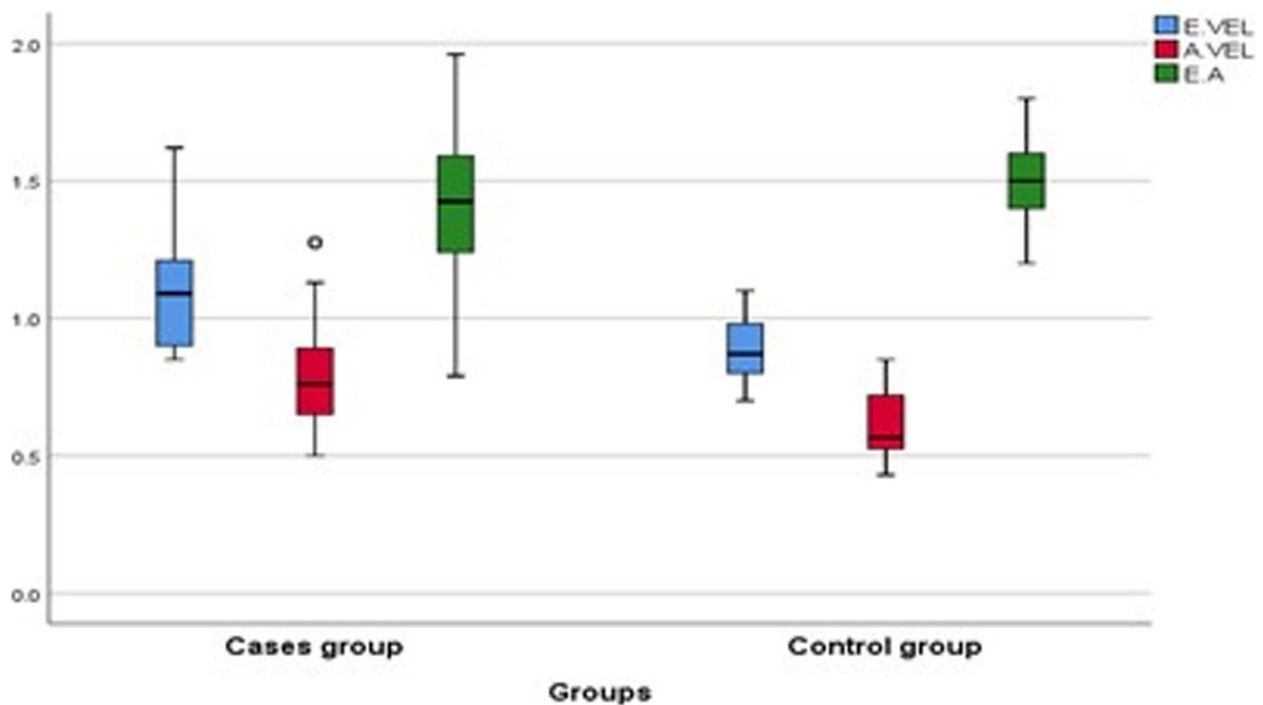
Speckle	Cases group (n = 34)	Control group (n = 20)	z	p value
Peak GLS (4CH) (%)	– 19.45(– 13.2, – 26.18)	– 23.61(– 19.46, – 27.88)	4.39	< 0.001*
Peak GLS (2CH) (%)	– 19.59(– 12.4, – 24.3)	– 23.65(– 19.36, – 27.4)	4.58	< 0.001*
Peak GLS (APLAX) (%)	– 19.53(– 15.2, – 28.1)	– 25.2 (– 19.9, – 28.33)	4.74	< 0.001*
HR APLAX (bpm)	107(70–170)	96(79–110)	2.85	0.004*
PSD Full (ms)	37.92(25.34–76.6)	45.45(7–119)	1.28	0.200
GS (avg)	– 19.98 (– 16, – 23)	– 24.40(– 19.82, – 25.9)	5.33	< 0.001*

Data expressed as median (min–max)

z Mann–Whitney U test

GLS Global longitudinal strain, 4CH 4 chamber view, 2CH 2 chamber view, APLAX Apical long axis, HR Heart rate, PSD Peak strain dispersion, GS Global strain, avg Average

\* Statistically significant



**Fig. 13** Box and whisker plot of PW Doppler

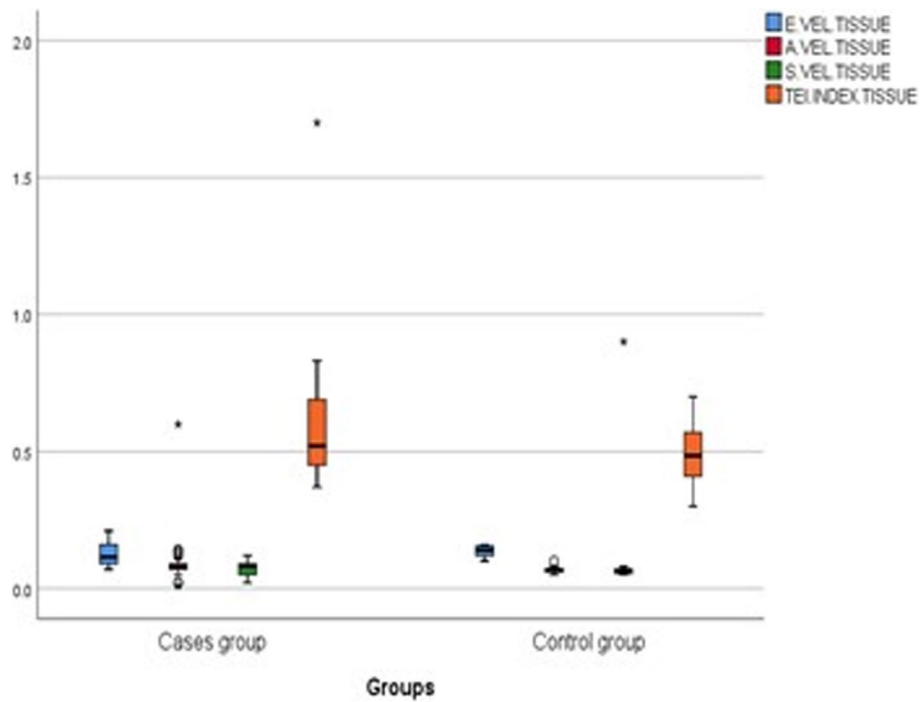


Fig. 14 Box and whisker plot of tissue Doppler

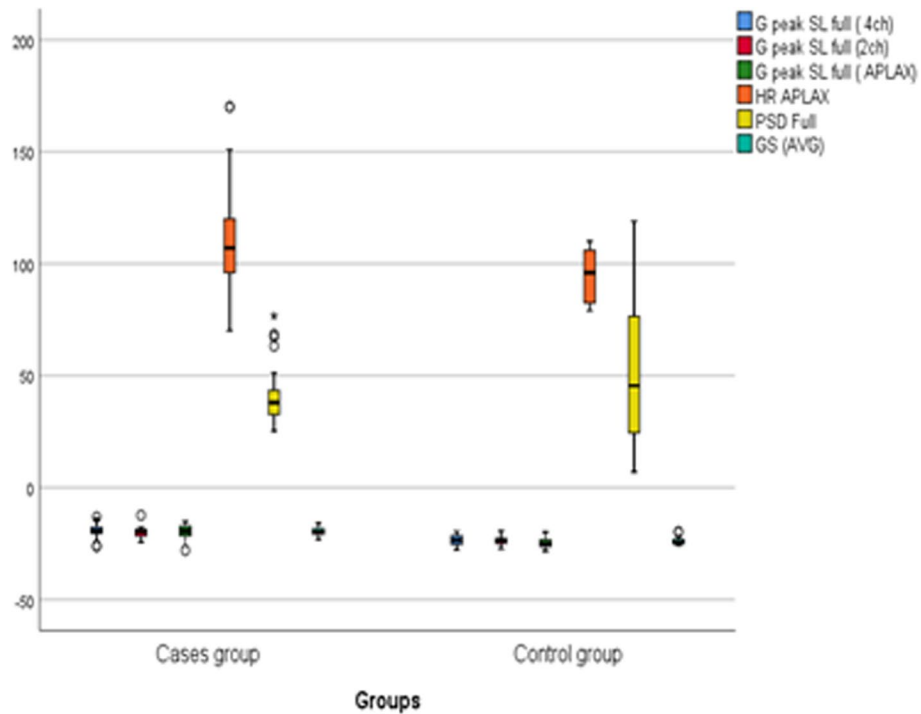


Fig. 15 Box and whisker plot of speckle tracking of LV

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Not applicable.

**Authors' contributions**

AB performed the clinical examination, did echocardiography, contributed to data interpretation, and drafted the work. OA shared in data interpretation and revised discussion. ME performed the statistical analysis and contributed to the interpretation of the results and writing the discussion. HA formatted the study design, rechecked the echocardiography of the sample of cases and control, and contributed to data interpretation and discussion revision. All authors have participated in drafting the manuscript. All authors read and approved the final version of the manuscript. All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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**Availability of data and materials**

All data generated or analyzed during this study are included in this published article and its supplementary information files could be obtained after communication with the corresponding author.

**Declarations****Ethics approval and consent to participate**

The study followed the Principles of the Declaration of Helsinki and was approved by the Ethical Review Committee of Kafrelsheikh University registered with approval code (MKSU 50–8–1) and informed written parental consent from all participants in the research.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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