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Left atrial Strain in Pediatric patients with hemodynamically significant PDA : Case- control study

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Abstract

Background: LA contractility controls LV filling and has a significant value in maintaining cardiac output even if the patient suffers from impaired relaxation or reduced compliance of LV . In case of impaired LV relaxation, the reservoir and pump phases take the upper hand in diastolic LV filling while reservoir phase decrease. LAS is the newest technique for direct evaluation of LA function and non-invasive assessment of LV diastolic function in pediatrics . Different echo views for imaging acquisition and different software packages and modalities of postprocessing analysis are now available

Aim of the work: We aimed to evaluate LAS in pediatric Patients with hemodynamically significant PDA that are going to percutaneous PDA closure.

Methods: This prospective controlled study was performed on 30 children divided in two groups (20 as cases and 10 as controls) for comparison of echocardiographic measurements. Conventional Echocardiography , Tissue doppler and Speckle tracking were done for all patients and measurement were compared.

Results: There was statistical significant difference (p value < 0.05) in LAS in reservoir phase and LAV maximum volume in PDA group indicating volume overload on LA and diastolic dysfunction of Left ventricle. This difference was not obtained using conventional echocardiographic parameters and Tissue doppler.

Conclusion: Left atrial speckle tracking in patients with congenital heart diseases like PDA is a useful tool that can detect diastolic dysfunction that couldn't be detected by conventional echocardiographic indices and tissue doppler and best view for LAS is 4 chamber view or biplane . LAS during reservoir phase could be a sole diagnostic parameter for left ventricle diastolic dysfunction.

Key Words: LAS; PDA; Echocardiography

Background:

Echocardiographic study of left ventricle (LV) filling pressure is crucial step in the evaluation of diastolic dysfunction . Most used echocardiographic indexes used for this purpose are produced with Doppler or Tissue Doppler functions and frequently have limitations due to angle dependence[1].

In adults, two-dimensional (2D) speckle tracking echocardiography (STE) has been used to Evaluate left atrium (LA) function and left atrial strain (LAS) . It is a novel technique to be used in clinical practice. LAS measurements can be obtained easily, are not angle dependent, related efficiently with invasive measurement of LV filling pressure and have a prognostic value in adults with heart failure, atrial fibrillation and after acute myocardial infarction [2]

Dysfunction and structural remodeling of the left atrium (LA) are significant components of cardiovascular diseases. It is important to detect these changes early to allow evaluating even preclinical diagnosis of ventriculardysfunction or valve disease. It helps also in the diagnosis of emerging atrial cardiomyopathy [3].

LA function consists of three phases, mainly: reservoir, conduit, and active pump. In the case of normal diastolic function, the relative contribution of the particularLA components into the left ventricular (LV) filling is as follows: reservoir 40%, conduit 35%, pump 25% [4] .

LA contractility controls LV filling and has a significant value in maintaining cardiac output even if the patient suffers from impaired relaxation or reduced compliance of LV . In case of impaired LV relaxation, the reservoir and pump phases take the upper hand in diastolic LV filling while reservoir phase decrease . This impaired phasic function of the LA was described in many cardiac pathologies like arrhythmia, mitral valve diseases and dilated cardiomyopathy [5]

LAS is the newest technique for direct evaluation of LA function and non-invasive assessment of LV diastolic function in adults . Different echo views for imaging acquisition and different software packages and modalities of postprocessing analysis are now available[6].

LAS studies are limited in congenital heart diseases and in Pediatric in general so the aim of this study was to evaluate LAS in pediatric Patients with hemodynamically significant PDA that are going to percutaneous PDA closure.

Aim of Work:

We aimed to evaluate LAS in pediatric Patients with hemodynamically significant PDA that are going to percutaneous PDA closure

Methods:

This study is a prospective analytical study on 20 infants and children in the Pediatric Cardiology Division of Specialized Pediatric Hospital, Cairo University, with audible PDA.

A control group consisting of 10 healthy infants and children was included in the study for comparison of echocardiographic measurements.

Inclusion Criteria:

Infants and children aged from 6 months to 18 years, weighing >6 kg with with hemodynamically significant PDA according to criteria in table 1. These patients underwent percutaneous PDA device closure.

Table 1: Comprehensive Grading Schema for HSPDA among older children ***(Backes et al, 2022)***

PDA size	Physiological symptoms
Silent or trivial	• "Silent" (inaudible) PDAs are asymptomatic* • No hemodynamic or anatomic sequelae • Normal exercise capacity • Normal renal, hepatic, and pulmonary function
Small	• Small left-to-right shunt, not HSPDA • No restrictions of exercise capacity
Mild/moderate	• Mild-moderate left-to-right or bidirectional shunt, HSPDA • Mild-moderate hemodynamic or anatomic sequelae (mild/moderate LAE and/or LVE, mild- moderate left ventricular dysfunction) • Mild or moderate hypoxemia/cyanosis • Mild or moderate PH • Potential for mild renal, hepatic, and pulmonary dysfunction

Large	• Large left-to-right, bidirectional, or right-to-left shunt • Severe hemodynamic or anatomic sequelae (severe LAE and/or LVE, moderate to severe left ventricular dysfunction) • Moderate or severe hypoxemia/cyanosis • Severe PH • Risk of Eisenmenger syndrome with PH and right-to-left shunting

HSPDA indicates hemodynamically significant PDA, defined as left atrial/ventricular enlargement and/or sustained pulmonary blood flow to systemic blood flow ratio (Qp/Qs) ≥1.5; LAE, left atrial enlargement; LVE, left ventricular enlargement; PDA, patent ductus arteriosus; and PH, pulmonary hypertension.

*Not all asymptomatic PDAs are silent.

Twenty five patients with hemodynamically significant PDA meeting inclusion Criteria were included in the study from November 2022 to January 2024 and pre-procedural Echocardiography was done for all of them , five of them were referred to surgical team for closure due to procedure complication .

Patients Evaluation:

All children were evaluated with good history data, full examination with concentration on weight and height and Local cardiac examination.

Investigations:

All children were submitted to routine investigations, Chest x ray, ECG, and a complete transthoracic echocardiography (TTE) using different echocardiographic modalities such as 2D TTE, tissue Doppler imaging (TDI), and 2D STE.

Equipment:

- **Machine**: Echocardiographic studies were performed 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 analysed using AFI software on the Equipment.

A. Conventional Echocardiographic examination

The examination was performed for all patients using the standard echocardiographic views and qualitative complete studies according to the American Society of Echocardiography guidelines. ***[7].***

B.Tissue Doppler Examination (TDE):

PW-TDI sample volume is placed at the level of the septal mitral annulus. Spectral tissue Doppler systolic wave S', and two retrograde waves, E' and A' wave . The MPI was calculated as Tei index=a′−b‘/b‘ where a‘ is the time interval from the end of the A'-wave to the onset of the E'-wave and b‘ the time from the onset to the end of the S‘-wave as illustrated in Figure 1.

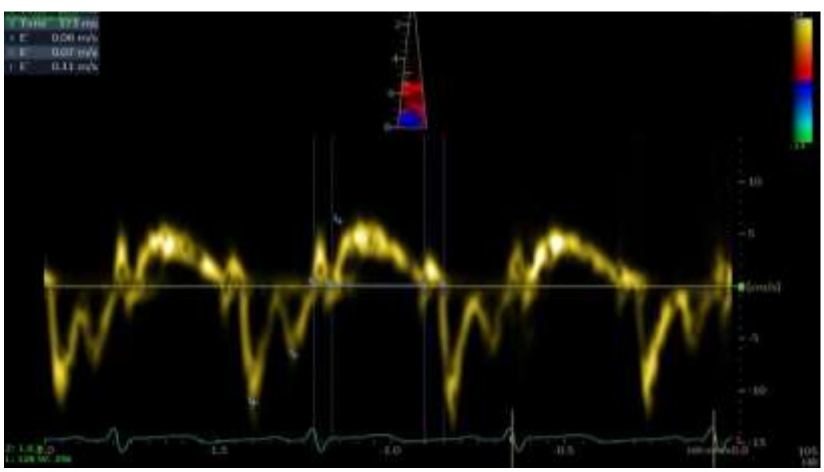

Figure 1: Tisssue Doppler of 1 .5 year old patient with PDA , TEI index 0.40

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. The 2D LA AFI function of the device was used to quantify global Left atrial strain and function . 2 views were obtained 4 chamber, 2 chamber **(Figures 2)**

The 2D Strain tracking was performed starting from a region of interest (ROI) defined at end-systole. 2D Strain analysis was integrated as the last step in the 2D auto left atrial quantification tool, which also included volume and atrial Ejection fraction measurements. The meshes created for these two measurements were used for the 2D Strain ROI. The 2D Strain ROI was automatically generated in the end-systolic frame and was built up from an endocardial and an epicardial mesh **.** The endocardial mesh was based on the one used for the the end-systolic volume measurement. The user could correct the ROI shape by placing attractor points to pull the nearby ROI border towards where the user wishes it to go from the tracking results.

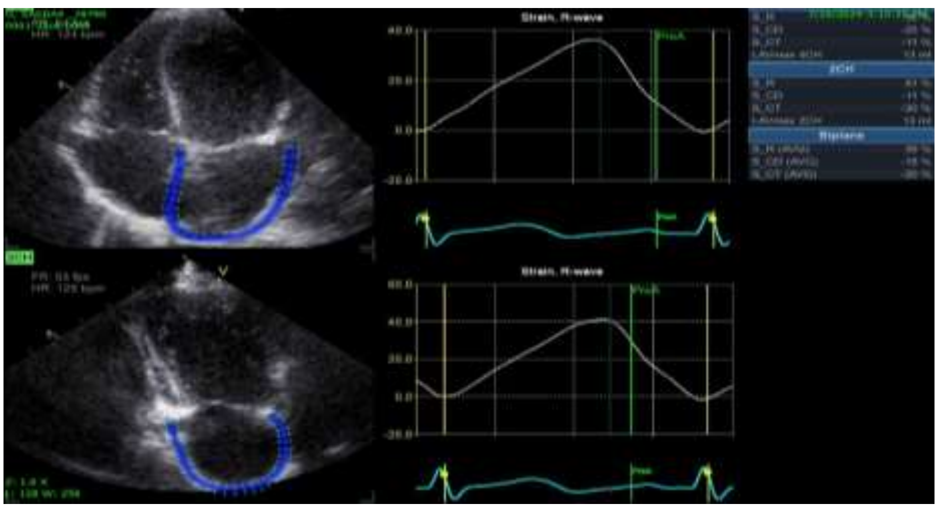

Figure 2: Left atrial strain calculated by LA AFI in 1 year old patient with hemodynamically significant PDA in Left atrial strain calculated by LA AFI in 4 chamber view and 2 chamber view and biplane.

Intra-observer and Inter-observer Variability:

To assess intraobserver variability, the same observer measured the 2D strain analysis of 10 randomly selected patients twice at an interval of 2 months to avoid recall bias. To assess interobserver variability, 2D strain measurements was performed by a second observer who was blinded to the results of the first observer.

ETHICS OF RESEARCH

The study followed the Principles of the Declaration of Helsinki and 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

Statistical analysis and data interpretation:

Data analysis was performed by SPSS software, version 25 (SPSS Inc., PASW statistics for windows version 25. Chicago: SPSS Inc.). Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for non-normally distributed data and mean± Standard deviation for normally distributed data after testing normality using Kolmogrov-Smirnov test. Significance of the obtained results was judged at the (≤0.05) level.

- Chi-Square , Fisher exact test , Monte Carlo tests were used to compare qualitative data between groups as appropriate
- Mann Whitney U test was used to compare between 2 studied groups for non-normally distributed data.
- Student t test was used to compare 2 independent groups for normally distributed data .
- Wilcoxon signed rank test used to compare between 2 studied periods for non-normally distributed data.

Results:

A sum of 20 cases fulfilled criteria of study were compared to 10 control cases, Regarding demographic data, there was statistical difference regarding weight and BSA in PDA group with p value <0.001* as illustrated in table 1

Table (1): comparison of demographic characters between studied groups

	Cases group (n=20)	Control group (n=10)	Test of significance	P value
Age / years	2(0.75-10)	3(4-12)	Z=1.5	0.24
Weight (kg)	10(5.2-30)	19(16-52)	Z=2.92	<0.001*
Height (cm)	89(68-137)	134(85-155)	Z=3.35	<0.001*

BMI (Kg/m2)	14.56±4.08	14.53±4.78	t=0.021	0.983
BSA	0.485(0.34-1.07)	0.85(0.61-1.47)	Z=3.21	<0.001*

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

*Z:Mann Whitney U test , t: Student t test , *statistically significant*

Regarding 2D conventional Echocardiographic data, There was no statistical difference between 2 groups regarding Left ventricle end diastolic diameter (LVIDD) and systolic functions in 2 groups were nearly equal . While There was no statistical difference in LA internal diameter between 2 groups, There was statistical difference in LA/AO ratio with p Value 0.001 indicating LA dilatation in PDA group as illustrated in table 2

Table (2): comparison of Conventional Echocardiographic finding in cases versus control

	Cases group (n=20)	Control group (n=10)	Z	P value
LVIDD	3.15(2.7-4)	3.42(2.3-3.94)	1.26	0.209
FS	34(29-76)	36.3(31-48)	0.727	0.467
EF	65(44-82)	68(60-80)	1.15	0.252
E/A	1.43(1.0-1.79)	1.55(1.2-1.8)	1.15	0.251
LA	1.9(1.6-2.5)	1.8(1.6-2.3)	1.07	0.284
AO	1.15(0.9-2.0)	1.65(1.2-2.5)	1.5	0.24
LA/AO	1.59(1.15-2.11)	1.15(0.8-1.4)	3.53	0.001*

Data expressed as median (min-max)

*Z:Mann Whitney U test , *statistically significant*

Regarding Tissue doppler comparison between 2 groups, there was no statistical difference observed in myocardial performance index (MPI) as illustrated in table 3 and figure 5

Table (3): comparison of TEI index between studied groups

	Cases group (n=20)	Control group (n=10)	Z	P value
TEI index	0.455(0.17-0.83)	0.485(0.35-0.70)	0.243	0.808

Data expressed as median (min-max)

*Z:Mann Whitney U test , *statistically significant*

Regarding 2D speckle tracking between 2 groups there was statistical significant difference between PDA group and control group regarding LV global strain with p value 0.001. There was also statistical difference in LA strain in reservoir phase in 4 chamber view with p value 0.001 and also in Biplane with p value 0.001, this finding was not observed in reservoir phase in 2 chamber view. Left atrial strain in conduit phase was affected in any view as illustrated in figure 3. LA strain in contraction phase was statistically significant higher in PDA group in 4 chamber view and biplane. Left atrial Maximum volume was statistically significant higher in PDA group with p value 0.001, 0.001, 0.03 in 4CH, 2CH and Biplane modes respectively as illustrated in table 4 and Figure 4

Table (4): comparison of 2D speckle tracking of Left Atrium between studied groups

	Cases group (n=20)	Control group (n=10)	Z	P value
Left Ventricle GS	-20.1(-24.3 , -17)	-24.1(-25 , -21.8)	3.81	0.001*
LA Strain Reservoir (4ch)	16(12-34)	37(13-47)	2.79	0.005*
LA Strain Conduit (4ch)	-14(-37, -1)	-21.5(-31, -16)	1.54	0.123
LA S Contraction (4ch)	-28(-37 , -9)	-17.5(-31 , -1)	2.24	0.025*
LA Vmax (4ch)	18(10-29)	11(9-34)	3.19	0.001*
LA S R(2ch)	33(11-51)	25(10-39)	1.37	0.172
LA S CD (2CH)	-10.5(-30.0 , -1.0)	-18(-26 , -12)	1.65	0.098
LA S CR (2CH)	-19(-51 , -4)	-12.5(-23 , -7)	1.43	0.152
LA V max (2ch)	25(10-33)	10(8-16)	3.31	0.001*
LA S R (Biplane)	25(1-39)	41(26-47)	3.89	0.001*

LA S CD (Biplane)	-13(-34 , -2)	-19(-28 , -15)	1.72	0.086
LA S CR (Biplane)	-23(-39 , -10)	-9.0 (-14 , -6.0)	4.1	0.001*
LA Vmax (Biplane)	13(8-29)	10(8-29)	2.2	0.03*

Data expressed as median (min-max)

*Z:Mann Whitney U test , *statistically significant*

Figur

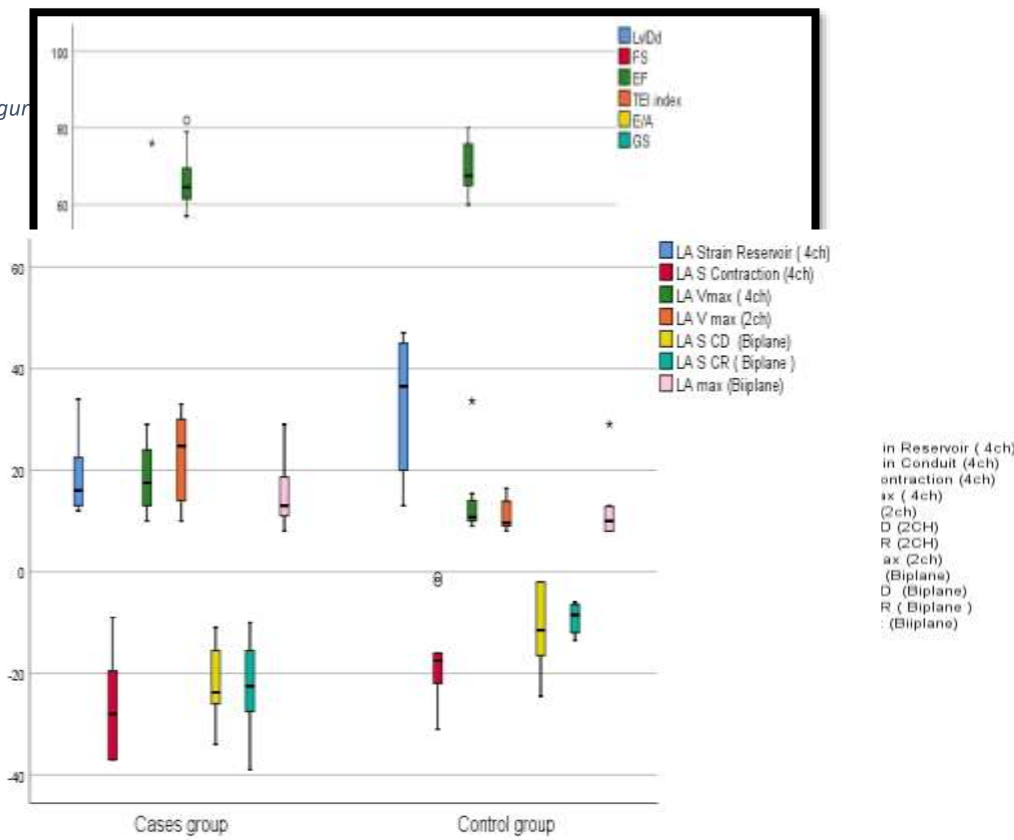

Figure 4: Box and Whisker Plot of statistically significant findings of LA speckle tracking

Figure 5: Box and Whisker plot of Speckle tracking finding Of 2D echocardiographic comparison and TEI index.

Discussion:

With review of literature, this is the first study that longitudinally assessed LAS measured by 2D STE in children with significant PDA . We had image standards for acquisition and postprocessing analysis and LAS Measurements feasibility and reproducibility.

The challenging in this study with widespread clinical application of LAS is the lack of standardization of image acquisition and postprocessing analysis, There are a lot of software packages and measurements to be applied. A recent consensus document tried make standard definitions and techniques for using LAS in adults. This may be needed in Pediatrics as the current data were obtained with different softwares and different methods of both image acquirement and postprocessing analysis [9].

In this study, we developed an LAS protocol for image acquisition and postprocessing analysis. We recommended that LAS should be computed from a biplane algorithm, which includes the apical 4-chamber and 2-chamber views, whereas assessment of LAS from an apical 3-chamber view should be avoided because the ascending aorta is difficult to separate from the atrial wall[10]. De Waal et al. computed LAS using a triplane algorithm, that included LAS from an apical 3-chamber view, although they the image acquired had needed further standardization, given the complexity of having good quality images. [11]

We observed excellent intraobserver reproducibility for LASr, LAScd and LASct and fair interobserver reproducibility. We feel that this was due to the protocol that was for image acquisition and postprocessing analysis. Our data on reproducibility are similar to that reported by De Waal et al. and Kutty at al. and confirm that within and between observer differences in LAS measurements may not be clinically relevant [10,11].

Although LAS is currently the best available non-invasive technique to directly assess LA function and indirectly assess LV diastolic function in adults, few data on LAS are available in pediatrics [1]. To our knowledge , there are two pediatric studies presented normal values of LAS in term neonates and older children. Kutty et al. and Ghelani et al. reported reference values of LAS in subjects with an age ranging from 3 days to 20 years and from 4 days to 20.9 years, respectively [9, 12].

In our study on cases with hemodynamically significant PDA who underwent percutaneous PDA closure, 2D echocardiographic findings were not significant as LVIDD between cases and control were statistically not significant. Also, systolic function of PDA group regarding Ejection fraction and fraction shortening were not affected. LA dimensions were not significantly different between cases and controls while LA/ AO ratio was statistically significant higher in PDA group indicating LA dilatation due to volume overload on LA due to increased pulmonary venous return. This was observed in study by Heuchan et al which indicted that pulmonary hyperperfusion is documented with a LA/Ao ratio of ≥1.5, an increased flow across the mean pulmonary artery and an elevated diastolic flow in the left pulmonary artery [13].

PW doppler findings between 2 groups were not statistically significant as E/A ratio p value between 2 groups was 0.25 and mean E/A ratio in case group was 1.45. In other studies, indicated that a mitral E/A ratio of >1.5 suggesting severe left heart pressure loading [14].

Tissue doppler was done to evaluate myocardial performance index (Tei index) which was not statistically different between 2 studied groups as p value was 0.8. In study by Zhou et al, he stated that Tei index of PDA children was higher than that of control group ($P<0.05$) before intervention [15].

Speckle tracking of left atrium in studied groups showed significant differences that were not observed by other indices in conventional Echocardiography and Tissue doppler. Although LVIDD and systolic function indices were not affected in PDA group, LV global strain was statistically significant between 2 groups indicating affected LV systolic function in hemodynamically significant PDA. Regarding left atrial strain there was statically significant decreased during reservoir phase in both 4 chamber view and biplane mode, this was not observed in 2 chamber view. This is compatible with previous studies as the optimal window to assess LAS is an apical, non-foreshortened, four-chamber view published in a consensus document of the European Association of Cardiovascular Imaging [16]. There are no data from other studies on LAS in PDA patients but there are published studies about data on PDA in preterm which documented similar results [11].Also, LA speckle was increased in contraction phase in 4 chamber view and biplane in PDA group and was statistically significant higher. This is contributed to increased volume overload on left atrium and diastolic dysfunction of left ventricle which increase left atrial strain during contraction phase that compensate for the decreased strain in reservoir phase. In a study by Karollina et al to assess diastolic dysfunction an Adults, they observed that Left atrial strain deteriorates according to severity of diastolic dysfunction and is proposed as prognostic marker of grades of diastolic dysfunction. A LAS in reservoir phase >35% allowed to differentiate patients with normal diastolic function with an accuracy of 72% [17].

LA max Volume obtained by 2D speckle tracking was increased in PDA group with statistically difference over control group indicating volume overload on LA and compatible with 2D echocardiographic findings.

Limitations:

Our study has several limitations. First, the number of subjects in the the two groups is relatively small to establish normal ranges. Further studies are needed to confirm our findings.

Secondly, the main limitation of 2D STE can be partial displacement of the speckles outside the imaging plane. Softwares packages are needed to be adjusted to be suitable for children less than 20 kgs.

Third, we didn't compare the results of LAS post PDA closure due to refusal of most of patients to perform functional echocardiography after closure and they were followed by conventional echocardiography only.

Conclusion:

Left atrial speckle tracking in patients with congenital heart diseases like PDA is a useful tool that can detect diastolic dysfunction that couldn't be detected by conventional echocardiographic indices and tissue doppler and best view for LAS is 4 chamber view or biplane . LAS during reservoir phase could be a sole diagnostic parameter for left ventricle diastolic dysfunction.

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