LUNG ULTRASOUND SCORE PREDICTS CHANGES IN ECHOCARDIOGRAPHIC PARAMETERS AFTER THE MANAGEMENT OF CHILDREN WITH CONGENITAL HEART DISEASE AND PULMONARY OVERFLOW

By

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ABSTRACT

Background: *Pulmonary overflow (PO) is a common finding in left-to-right shunting congenital heart diseases (CHD). B-line artifacts are seen on lung ultrasound in the presence of extravascular lung water.*

Objective: *We aimed to investigate the feasibility of lung ultrasound (LUS) to monitor changes in extravascular lung water after treatment of PO in children with CHD and compare LUS score results with echo parameters and management protocol.*

Patients and methods: *A cross-sectional study was conducted over 33 children with CHD and PO. Patients were subdivided into 3 groups according to management: percutaneous catheter closure (n=15), surgery (n=10), and medical treatment (n=8). Pulmonary congestion was identified using B-lines in LUS and/or chest X-ray (CXR). Twelve lung zones were scanned to calculate the B-line score. Changes were compared before- and after- management to monitor response.*

Results: *Pre-intervention, 74% and 24% of patients showed moderate and severe lung congestion, respectively. Patients with severe LUS scores showed significantly higher Qp:Qs ($p<0.001$), LA/Ao ($p=0.00$), LVEDd ($p<0.001$), Rt & Lt MPI ($P<0.001$). LUS score was significantly higher among patients referred for surgery ($p=0.001$). Post-intervention, all patients showed significant decline in LUS score ($p<0.001$). It was positively correlated with mean decline in Qp:Qs ($r=0.33$, $p=0.007$) & LA/Ao (r=o.72, $p<0.001$) and negatively correlated with mean increase in EF% ($r= -0.31$, $p=0.009$) and FS% ($r= -0.36$, $p=0.006$). Mean LUS score decreased significantly post-catheter closure ($p=0.03$).*

Conclusion: *LUS can detect severity of Pulmonary overflow (PO) in children with CHD. Also, LUS score correlated with hemodynamic changes before and after management providing an additional tool for accurate decision-making.*

Keywords: *ultrasound, pulmonary congestion, B-lines, pulmonary abnormalities, cardiac intervention, lung water.*

INTRODUCTION

Children with congenital heart disease (CHD) often exhibit respiratory symptoms. This may reflect abnormalities in lung dynamics due to increased extravascular lung water (EVLW) or an underlying lung infection **(Rodriguez-Fanjul et al., 2016) (Apostolopoulou, 2017)**. Early and accurate detection of pulmonary complications is pivotal to guiding successful treatment **(Assaad et al., 2018) (Wu et al., 2018)**. In recent years, lung ultrasound (LUS) has been increasingly used for diagnosing multiple pulmonary abnormalities **(Grune et al., 2020) (Tripathi et al., 2019) (Ford et al., 2107)**. Pulmonary overflow (PO) is a common finding in left-to-right shunting congenital heart diseases (CHD) **(Apostlolopoulou et al., 2017) (Wu et al., 2018)**. Therapeutic goals include alleviation of symptoms and correcting underlying cardiac defects. Both clinical and chest x-ray (CXR) findings are often late signs **(Tripathi et al., 2019) (Touw et al., 2018) (Ford et al., 2017)**. A recent study revealed that LUS can reliably estimate lung water **(Torino et al., 2021)**. Interstitial pulmonary congestion is viewed in LUS as a B-line acoustic artifact **(Lichtenstein et al., 1997) (Soldati et al., 2009)**. Echocardiography measurements are essential in clinical decision-making in children with structural cardiac defects **(Abel Aal et al., 2021)**. Hemodynamic congestion due to increased left ventricular end-diastolic pressure can be monitored via multiple parameters, described as surrogates of PO **(Picano et al., 2018)**. The pulmonary to systemic blood flow ratio (Qp/Qs) signifies lung plethora if >1.5:1. Also, ratio of the left atrium to the aortic annulus (LA/Ao) as well as left ventricular end-diastolic (LVED) dimensions identify LA enlargement predicting increased pulmonary blood flow due to left heart loading **(Rossouw et al., 2013)**. Few studies evaluated diagnostic utility of LUS to assess PO in children with CHD **(Rodriguez-Fanjul et al., 2016)**

(Wu et al., 2018) (Kaskinen et al., 2017) (Zhao et al., 2020).

The aim of this work was to investigate the feasibility of lung ultrasound (LUS) to monitor changes in extravascular lung water after treatment of PO in children with CHD and to compare LUS score results with echocardiographic parameters and management protocol.

ETHICAL CONSIDERATIONS

Ethical approval: This study was performed in line with the principles of the Declaration of Helsinki 1975. Approval was granted by the Ethics Committee of human experimentation of Ain shams university (FMASU MS726/2021).

Consent to participate: Informed consent was obtained from parents and legal guardians of studied patients.

Competing Interests: The authors have no relevant financial or non-financial interests to disclose.

Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Confidentiality: All the data of the study are confidential, and the patient has the right to keep it.

The patient has the right to withdraw from the study at any time.

Acknowledgments: The authors are indebted to the patients and their guardians who agreed to participate in the study.

SAMPLE SIZE CALCULATION

This was an exploratory study. No sample size was calculated.

PATIENTS AND METHODS

Study design:

This was a cross-sectional study that included 33 children (20 females and 13 males) diagnosed with congenital cardiac defects associated with increased pulmonary blood flow. They were recruited from the pediatric cardiology clinic, children's hospital, Ain shams university from January to July 2022. Patients were collected by consecutive random sampling method.

Inclusion criteria: Patients with confirmed echo diagnosis of CHD with increased pulmonary blood flow.

Exclusion criteria: Neonates, children with underlying primary lung disease, concurrent infection, or defects with pulmonary oligemia were excluded from the study.

They were further subdivided into 3 groups according to the decided management protocol: **Group 1:** for surgery (n=10), **Group 2:** for Catheter device closure (n=15), and **Group 3:** for symptomatic medical treatment (n=8).

All patients were subjected to the following:

I. Detailed medical history focusing on demographic data, symptoms, medications, and previous operations.

II. Clinical examination: Thorough examination of the heart and lungs was performed.

III. Radiology work-up:

Our patients initially performed transthoracic LUS and echocardiography (same day of recruitment) and 1 month later, after the assigned intervention.

1- Transthoracic lung ultrasound:

B-mode ultrasonography was performed using a GE ultrasound system (LOGIQ P9) using multifrequency linear/convex probe (7-12MHz). Measurements were taken by radiologist with experience in lung ultrasound. The sonographer was blinded to CXR and clinical findings. Chest was divided into 6 anterior and 6 posterior quadrants. B-lines were defined as a hyperechoic comet tail artifact arising from the pleural line, moving with lung sliding. In each scanning area, B-lines were counted. LUS score was quantified by summing partial scores for each area. Degree of lung involvement was classified into four categories: Trivial-none (LUS-score = 0–6), Mild (LUS-Score = 6–12), Moderate (LUS-Score = 13–24), Severe (LUS-Score > 24) [17].

2- Transthoracic Echocardiography:

Transthoracic echocardiography was performed using cardiac ultrasound unit device model (Vivid E95 ultrasound system, General Electric, Vingmed, Horten, Norway) with probe M5Sc by a specialized pediatric echocardiographer. Patients were evaluated with: 2D, M-mode echocardiography, continuous, pulsed, and color Doppler (Lopez et al., 2010). The following parameters were measured: ejection fraction (EF%), fractional shortening (FS%), pulmonary to systemic blood flow ratio (QP/QS), left and right ventricle myocardial performance index (MPI), left atrium to aortic annulus diameter ratio (LA/AO), and left ventricular end-diastolic dimension (LVEDd) (cm).

Statistical Methods:

Data management and statistical analysis was done using SPSS version 23; SPSS Inc., Chicago, IL, USA was used. Descriptive data were expressed as mean ± standard deviation (SD), range, median and interquartile range (IQR), number, and percentages. The analytical statistics used were Chi-square, paired t-test, independent sample t-test, one-way ANOVA, post hoc, and Spearman correlation coefficients. P-value <0.05 was considered significant.

RESULTS

The results of our study summarized in the following tables and figures:

Table (1): Demographic and clinical characteristics of studied patients

Variable		N=33
Age (years)	Median (IQR) Range	1.5 (0.5 -3.5) 0.25 -16
Sex, n (%)	Male Female	13 (39.4%) 20 (60.6%)
BMI (kg/m2)	Mean±SD Range	13.96±1.06 12.2-15.42
Type of Congenital heart defect, n (%)	VSD PDA ASD AV CANAL TGA Truncus arteriosus TAPVR Single ventricle	10 (30.3%) 7 (21.2%) 6 (18.2%) 3 (9.1%) 3 (9.1%) 2 (6.1%) 1 (3%) 1 (3%)
Pulmonary overflow frequency using LUS, n (%)	Positive Negative	33 (100%) 0
Pulmonary overflow frequency using CXR, n (%)	Positive Negative	28 (84.8%) 5 (15.2%)

Table (1) shows relevant demographic data and type of congenital defects in the studied participants. Pre-intervention, LUS, and CXR were performed. 100% of cases (n=33) had PO, with 76% (25/33) showing moderate and 24% (8/33) severe lung involvement. In 15% of cases (8/33) CXR was free.

Table (2): Comparison between patients with moderate and severe lung congestion as regards echo parameters before intervention

Echo parameters before management		LUS severity score before intervention Moderate (13-24) No. = 25	Severe > 24 No. = 8	Test value	P-value
EF%	Mean±SD	63.80±4.31	58.38±2.39	3.373	**0.002**
	Range	55–75	56–63		
FS%	Mean±SD	31.84±6.18	35.88±4.64	-1.692	0.101
	Range	26–45	29–45		
Rt MPI	Mean±SD	0.40±0.03	0.65±0.12	-9.558	**<0.001**
	Range	0.37–0.49	0.45–0.81		
Lt MPI	Mean±SD	0.37±0.02	0.47±0.07	-6.770	**<0.001**
	Range	0.34–0.4	0.39–0.58		
QP/QS ratio	Mean±SD	2.87±0.95	5.26±0.23	-6.963	**<0.001**
	Range	1.57–4.33	4.92–5.61		
LA/AO ratio	Mean±SD	1.68±0.13	2.18±0.08	-9.877	**<0.001**
	Range	1.36-1.89	2.06-2.31		
LVEDd (cm)	Mean±SD	4.31±0.61	5.51±0.20	-5.421	**<0.001**
	Range	3-5.4	5.2-5.8		

EF: Ejection fraction; FS: Fractional shortening; MPI: Myocardial performance index; QP/QS: ratio of Pulmonary-to-Systemic blood flow; LA/AO: ratio of Left atrial to aortic annulus dimension; LVEDd: left ventricular end diastolic dimension.
•: Independent Sample t-test

Table (2) shows that patients with severe PO (n=8), before management, showed significantly increased mean Qp:Qs ratio (p<0.001), LVEDd (p<0.001), and LA/Ao ratio (p<0.001) when compared with those with moderate lung involvement (n=25). Also, they showed bilateral ventricular dysfunction as evidenced by a significantly higher mean Rt MPI index (p<0.001), Lt MPI index (p<0.001) and lower mean EF% (p=0.002).

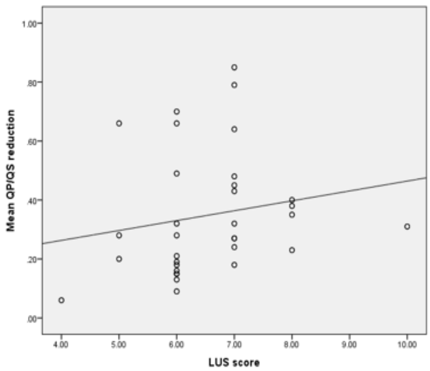

Fig. 1: Correlation between LUS score and mean QP/QS ratio reduction

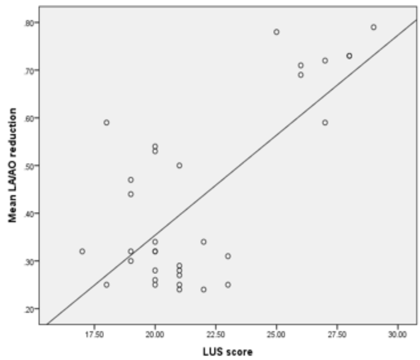

Fig. 2: Correlation between LUS score and mean LA/AO reduction

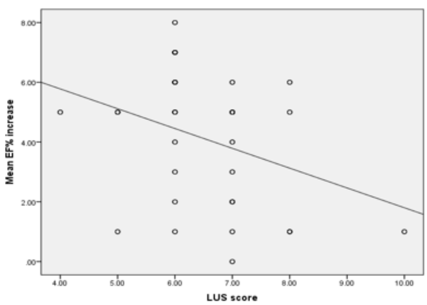

Fig. 3: Correlation between LUS score and mean EF%

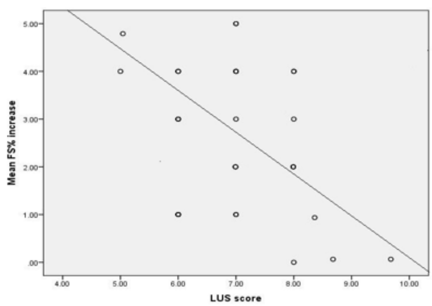

Fig. 4: Correlation between LUS score and mean FS %

Table (3): Comparison between echo parameters, LUS severity score, and degree of lung involvement in all patients before and after intervention

All patients		Pre-intervention	Post-intervention	Difference	Test value•	P-value
		No. = 33	No. = 33	No. = 33		
EF%	Mean±SD	62.48±4.56	66.58±4.68	4.09±2.21	-10.619	**<0.001**
	Range	55–75	55–76	0–8		
FS%	Mean±SD	32.82±6.04	35.36±5.23	2.55±1.50	-9.736	**<0.001**
	Range	26–45	29–45	0–5		
Rt MPI	Mean±SD	0.46±0.12	0.39±0.08	0.07±0.05	-8.116	**<0.001**
	Range	0.37–0.81	0.34–0.62	0.02–0.22		
Lt MPI	Mean±SD	0.39±0.06	0.34±0.04	0.05±0.02	-12.389	**<0.001**
	Range	0.34–0.58	0.3–0.48	0.02–0.13		
QP/QS	Mean±SD	3.45±1.33	3.10±1.35	0.35±0.21	-9.596	**<0.001**
	Range	1.57–5.61	1.48–5.33	0.06–0.85		
LA/AO	Mean+SD Range	1.80+0.25 1.36-2.31	1.37+0.17 0.97-1.64	0.43+0.19 0.24-0.79	13.026	**<0.001**
LVEDd (cm)	Mean+SD Range	4.60+0.75 3-5.8	3.99+0.61 2.9-5.1	0.67+0.26 0.2-1.3	9.442	**<0.001**
LUS score	Mean±SD	21.85±3.28	15.30±3.57	6.55±1.12	-33.555	**<0.001**
	Range	17–29	11–23	4–10		
Degree of lung involvement	Mild (6-12)	0 (0.0%)	6 (18.2%)	–	14.077*	**0.001**
	Moderate (13-24)	25 (75.8%)	27 (81.8%)	–		
	Severe (> 24)	8 (24.2%)	0 (0.0%)	–		

EF: Ejection fraction; FS: Fractional shortening; MPI: Myocardial performance index; QP/QS: ratio of Pulmonary-to-Systemic blood flow; LA/AO: ratio of Left atrial to aortic annulus dimension; LVEDd: left ventricular end diastolic dimension.
•: Paired t-test *: chi-square test

Table (3) shows that post-intervention, mean LUS score decreased significantly in all patients compared to that calculated pre-intervention (p <0.001). 18% (6/33) showed mild pulmonary congestion. Also, LUS score correlated positively with mean decrease in QP/QS (r=0.33, p=0.007) **(Figure 1)** and LA/Ao ratio (r=o.72, p<0.001) **(Figure 2)** and was negatively correlated with mean increase in EF% (r= -0.31, p=0.009) **(Figure 3)** and FS% (r=-0.36, p=0.006) **(Figure 4)**.

Table (4): Comparison between management protocols as regards mean LUS score before and after intervention

LUS score		Medical No. = 8	Cath No. = 15	Surgical No. = 10	Test value	P-value
Before intervention	Mean ± SD Range	21.25±2.31 18 -25	20.20±1.26 17 - 22	24.80±4.13 18 -29	9.186•	**0.001**
After intervention	Mean + SD Range	15.38±2.56 13 – 21	13.13±1.06 11 – 15	18.50±4.38 12 – 23	11.076•	**<0.001**

LUS: lung ultrasound, cath: catheter defect closure
•: One Way ANOVA test & Post Hoc test: Tukey's test

Table (4) demonstrates that mean LUS score before intervention was significantly higher among patients who were referred for surgery (p=0.001).

Table (5): Comparison between management protocols as regards mean amount of change recorded after intervention in echo parameters and LUS score

Amount of change		Medical No. = 8	Cath No. = 15	Surgical No. = 10	Test value·	P-value
Mean EF% Increase	Mean±SD	4.13±1.96	3.87±2.20	4.40±2.59	0.166	0.848
	Range	1–6	0–7	1–8		
Mean FS% Increase	Mean±SD	2.25±1.91	2.60±1.45	2.70±1.34	0.207	0.814
	Range	0–5	0–5	1–4		
Mean Rt MPI Reduction	Mean±SD	0.05±0.01	0.04±0.01	0.13±0.05	25.881	**<0.001**
	Range	0.03 - 0.07	0.02 - 0.07	0.08 - 0.22		
Mean Lt MPI Reduction	Mean±SD	0.04±0.01	0.05±0.02	0.06±0.03	2.222	0.126
	Range	0.03 - 0.07	0.02 - 0.08	0.03 - 0.13		
Mean QP/QS ratio Reduction	Mean±SD	0.38±0.23	0.29±0.15	0.40±0.26	0.978	0.388
	Range	0.06 - 0.7	0.09 - 0.64	0.18 - 0.85		
Mean LA/AO ratio Reduction	Mean±SD	0.36±0.19	0.35±0.10	0.62±0.17	11.571	**<0.001**
	Range	0.25-0.78	0.24-0.54	0.32-0.79		
Mean LVEDd Reduction (cm)	Mean±SD	0.66±0.32	0.66±0.30	0.69±0.14	0.041	0.960
	Range	0.2-1.3	0.3-1.3	0.5-0.9		
LUS score Reduction	Mean±SD	5.88±1.13	7.07±1.10	6.30±0.82	3.889	**0.031**

EF: Ejection fraction; FS: Fractional shortening; MPI: Myocardial performance index; QP/QS: ratio of Pulmonary-to-Systemic blood flow; LA/AO: ratio of Left atrial to aortic annulus dimension; LVEDd: left ventricular end diastolic dimension.
•: One Way ANOVA test & Post Hoc test: Tukey's test

Table (5) shows that mean total LUS score decreased significantly in patients who underwent percutaneous catheter closure compared to those who were assigned to a surgical procedure or medical management protocol (p=0.03). However, mean right ventricular MPI index and mean LA/AO ratio showed a significant decline following surgical intervention (p=0.00).

DISCUSSION

This study was conducted on infants and children with CHD and increased pulmonary blood flow. The increased pulmonary artery pressure and pulmonary venous pressure lead to pulmonary congestion, which results in increased pulmonary interstitial fluid **(Mathews et al., 2010)**. When EVLW increases, thickened alveolar septa and fluid in alveoli result in emergence of multiple B-lines in LUS. Our data point out that using a quantitative LUS score can evaluate PO severity, guide, and monitor effect of therapeutic measures, thus, decreasing CXR exposure. LUS score can also predict hemodynamic effects of the cardiac lesion providing clinicians with an additional tool for better decision-making. Ricci et al., 2014 found a good correlation between B-lines in LUS and PO in a group of cardiac patients. Previous studies **(Rodriguez-Fanjul et al., 2016) (wu et al., 2018) (Zhao et al., 2020) (Raimondi et al., 2018)** used various semi-quantitative LUS scores to demonstrate PO severity in children with CHD. In this study, LUS B-lines were detected in 100% of cases. However, only 85% showed positive CXR Kerley B lines. This was against the findings of **Bitar et al., 2015** and **Moustafa et al., 2017** who reported B profile in 47/61 (77%) and 27/60 (45%) of patients, respectively. In our work, we included only patients with confirmed pulmonary congestion using LUS or CXR. Our findings were consistent with **Zho et al., 2020** who concluded that LUS could detect an increase in B lines before CXR. In their study, **Touw et al., 2018** and **Ford et al., 2017** also stated that LUS was better than CXR and clinical examination in detecting multiple respiratory complications. The increased pulmonary blood flow resulting from underlying cardiac defect promotes enlargement of left atrium and both ventricles but not of the aorta. Previous studies **(Lewis et al., 1976)** reported a good correlation between Qp/Qs ratio obtained at cardiac catheterization and echocardiographic LA/Ao ratio. LA/Ao was considered by some authors as a sensitive echocardiographic parameter for identifying LA enlargement in children **(Brown et al., 1974) (Lester et al., 1979)**. Moderate and severe degrees of pulmonary congestion were observed in 76% and 24% of patients, respectively, in this study. Comparing the echocardiographic parameters of both groups showed that those with higher B-lines showed higher mean Qp:Qs, LA/Ao ratio, and increased mean LVED dimension. This agrees with Zhao et al., 2020 who found that LUS score was significantly higher in those with PDA non-closure and was correlated with LA/Ao ratio. There was a significant difference in mean total LUS score in all patients before- and after-intervention. This agrees with **song et al., 2018** and **Cantinotti et al., 2019**. **Alonso-Ojembarrena et al., 2020** also reported improved LUS scores following using diuretics in LBW infants. Similarly, in adults, **Cortellaro et al., 2017** found that LUS can monitor the response after 24 hours from starting treatment of cardiogenic pulmonary edema. Several studies addressed the performance of echocardiographic parameters following CHD correction **(Abdel Aal et al., 2021) (Salehian et al., 2005) (Zhang et al., 2008)**. Hence, a significant reduction in echocardiographic parameters 1-month after intervention was anticipated. This study was unique in detecting a significant correlation between changes in LUS score and measured echo parameters. This indicates that changes in PO detected by LUS parallel changes in hemodynamic parameters. Thus, LUS can be a promising tool to help clinicians, especially in limited resource settings, to objectively monitor cardiac patients in absence of trained cardiac sonographer. This was the first study to compare different therapeutic interventions in children with CHD and PO. Intriguingly, patients who were referred for surgery were found to have significantly higher mean LUS score. Thus, classification of PO in children with CHD using LUS can provide an overview of disease severity and can guide therapy. Patients selected for percutaneous defect closure showed a higher significant mean reduction in B-lines score than those referred for surgery. This can be explained by our heterogenous population and that EVLW can occur following cardiopulmonary bypass. However, improved hemodynamic congestion, as reflected by decreased right ventricle dysfunction and left ventricular dimensions, was more pronounced after surgical intervention. LUS with cardiac ultrasound provide useful tools for prognostic evaluation of patients with CHD following intervention.

CONCLUSIONS

LUS can detect severity of Pulmonary overflow (PO) in children with CHD. Also, LUS score correlated with hemodynamic changes before and after management providing an additional tool for accurate decision-making.

RECOMMENDATION

Lung ultrasound Score can be used to monitor changes in pulmonary overflow in children with congenital heart diseases before and after interventions. Further studies are required on larger scale to confirm our findings.

STUDY LIMITATIONS

The main limitations of this study are small sample size, heterogeneity of studied subjects, LUS and echocardiography were performed by a single operator. Quantitative MRI, the gold standard for diagnosing increased PBF, was not performed.

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