

# Point-of-care diaphragm ultrasound: an objective tool to predict the severity of pneumonia and outcomes in children

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## Abstract

**Background:** Pneumonia is one of the most common serious infections in children. Scoring systems have been adopted to quantify the severity of the disease, but they were based on clinical findings that can vary according to the subjective assessment of the clinician. We hypothesized that diaphragm ultrasound (DUS) parameters may be a new useful tool to objectively score the severity of the disease and predict outcomes in children with pneumonia. **Methods:** Children diagnosed with pneumonia, aged between 1 month and 18 years, were prospectively evaluated in the pediatric emergency department. The Pediatric Respiratory Severity Score was used to indicate the severity of the disease and DUS was performed. Diaphragm thickness at the end of inspiration and expiration, thickening fraction (TF), diaphragm excursion, inspiratory slope (IS), expiratory slope (ES), and total duration time of the respiratory cycle were calculated. **Results:** There were 96 patients enrolled in the study. Inspiratory slope and ES measurements had positive correlations with respiratory rate and length of stay in the hospital and negative correlations with oxygen saturation levels. Furthermore, TF values were negatively correlated with respiratory rate and length of stay in the emergency department. Patients with higher clinical scores had increased IS and ES and decreased TF values. **Conclusion:** Diaphragm ultrasound can be a promising and useful tool to assess diaphragmatic dysfunction in patients diagnosed with pneumonia. Diaphragm parameters, especially TF, IS, and ES, may provide objective and reliable information to predict the severity of the illness, the need for respiratory support, and outcomes.

## Point of care diaphragm ultrasound: an objective tool to predict the severity of pneumonia and outcomes in children

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**Running head:** Point of care diaphragm ultrasound in children with pneumonia

## INTRODUCTION

Pneumonia is known as one of the most common serious infections in the pediatric population worldwide. Pneumonia-related mortality is rare in developed countries, but in developing countries, it is still one of the major causes of mortality in childhood <sup>1,2</sup>. Most children can be treated as outpatients, although hospitalization rates may vary from 19% to 69% in emergency departments <sup>3,4</sup>. Although the diagnosis is based on clinical parameters, there are no highly specific criteria for diagnosis. Chest X-ray (CXR) is not routinely recommended, while the World Health Organization recommends CXR in children who are clinically diagnosed with severe pneumonia at tertiary centers. The level is 90% for children with suspected pneumonia <sup>5,6</sup>. The severity of the disease can be predicted using demographic characteristics, risk factors, and clinical parameters, but this may be difficult in an emergency department. Scoring systems have been adopted to quantify the severity of the disease and prognosis, but they were based on clinical findings that can vary according to the subjective assessment of the clinician <sup>7</sup>. Biomarkers have been found to be useful in diagnosis, in differentiating bacterial or viral etiology, and in predicting severity or prognosis recently, but they are expensive when evaluated in combination to reflect various pathophysiological pathways <sup>8,9</sup>. Therefore, it is crucial to develop an objective and useful parameter to demonstrate the severity of the disease and outcomes.

Point-of-care lung ultrasound (LUS) has increasingly been used in pediatric emergency settings recently. It is easy to perform, rapid, cost-effective, repeatable without limitations, and radiation-free. In a meta-analysis, LUS was found to be more sensitive and specific compared to CXR for diagnosing pneumonia in children <sup>10</sup>. Another meta-analysis demonstrated that LUS had sensitivity of 96%, specificity of 93%, positive likelihood of 15.3, and negative likelihood of 0.06 when compared to CXR alone or in combination with clinical and laboratory findings and CXR <sup>11</sup>. Jones et al. also showed that the use of LUS reduced CXR levels over 38% and shortened the length of stay in the emergency department <sup>12</sup>. Lung ultrasound seems to be a highly promising tool for pneumonia diagnosis in pediatric emergency departments.

The diaphragm is the main respiratory muscle and diaphragmatic dysfunction may cause severe problems for respiration <sup>13</sup>. Diaphragm ultrasound has been used to evaluate diaphragmatic fatigue after cardiac surgery or to predict extubation success from mechanic ventilators in adult and pediatric intensive care units recently <sup>14-16</sup>. However, there is no study providing information on the evaluation of DUS in children with the diagnosis of pneumonia. We hypothesized that DUS parameters could be a new useful tool to objectively score the severity of the disease and predict outcomes in previously healthy children with pneumonia in the emergency department.

## MATERIALS AND METHODS

### Study population

We conducted a prospective study between December 2018 and May 2019. The study protocol was approved by the Ethics Committee of the Dokuz Eylul University Faculty of Medicine. Fully informed consent was obtained from the parents or legal guardians of each participant before enrollment in the study.

### Study design

The study was performed in the pediatric emergency department of the Dokuz Eylul University Faculty of Medicine. Previously healthy children between 1 month and 18 years of age were included. Patients were excluded if they had life-threatening diseases requiring immediate intervention; chronic pulmonary, cardiac, or neuromuscular diseases; diaphragmatic hernia; diaphragm paresis; chest wall abnormalities; genetic disorders; or history of cardiac/thoracic operation or prematurity (<34 gestational week). The patients who presented to the pediatric emergency department with suspicious clinical symptoms, physical examination

findings, and infiltration on CXR (if performed) were considered as having suspected pneumonia and all of them were examined by LUS. If pneumonia was confirmed by LUS, then the patients were enrolled in the study and DUS was performed. The Pediatric Respiratory Severity Score (PRESS) was used to indicate the severity of the disease. This scoring system comprises respiratory rate, wheezing, use of accessory muscles, refusal to feed, and oxygen saturation SpO<sub>2</sub> of <95% in room air. Each parameter was scored with 0 or 1 point and the total score was classified as mild (0–1 points), moderate (2–3 points), or severe (4–5 points)<sup>17</sup>. The demographic, clinical, and laboratory data of the patients were recorded together with LUS findings, DUS parameters, and PRESS scores by a pediatric emergency fellow at admission. Vital findings were monitored by a nurse and the patients were evaluated by a pediatric assistant and a pediatric emergency fellow. Length of stay in the pediatric emergency department, need for hospitalization, and length of total stay in the hospital were recorded.

## Statistical analysis

Statistical analyses were performed using SPSS software version 22.0 for Windows. Data were presented as means with standard deviations (SDs) or medians with interquartile ranges (IQRs). The Mann–Whitney U test was used to compare non-parametric variables and Student’s *t*-test and one-way analysis of variance (ANOVA) testing were used for parametric data. Correlations between DUS parameters and clinical scores were assessed with Spearman’s rank correlation coefficient. Cut-off values of predictors were calculated using a receiver operating characteristic (ROC) curve. Values of  $p < 0.05$  were considered statistically significant.

## Ultrasound examination

Our ultrasound examination was performed using a Philips ClearVue 350 portable system with an L12–4 MHz linear transducer by a single well-trained pediatric emergency fellow. Lung ultrasound evaluation was performed using the methodology previously described by Copetti et al.<sup>18</sup>. Diaphragm ultrasound was performed when the patient looked calm, was not coughing, and was not crying. Subjects were imaged in the supine position. If the infiltration was unilateral, the pathological side was evaluated, while if the lungs were bilaterally affected, then the mean of the right and left side measurements was calculated. The average values of three consecutive cycles were recorded. The transducer was positioned between the 9<sup>th</sup> and 10<sup>th</sup> intercostal spaces in the mid-axillary/mid-clavicular line in the coronal plane. First, the 2-dimensional mode was used to achieve the best view between the two echogenic parallel lines of the pleura and the peritoneum. Then M-mode imaging was used to obtain all DUS parameters. During M-mode, a normally functioning diaphragm is detected as an echogenic line that moves freely during inspiration and expiration. During inspiration, the normal diaphragm moves caudally toward the transducer, as an upward flexion. During expiration, the diaphragm moves cephalad, away from the probe, as downward flexion. The diaphragm excursion was measured on the vertical axis, tracing from the baseline to the point of the maximum height of inspiration on the graph. Diaphragm thickness (TD) was determined by measuring the vertical distance between the midpoints of the pleural and peritoneal layers at the end of inspiration and expiration<sup>19</sup>. The thickening fraction was calculated as (TEI – TEE)/TEE, where TEI is diaphragm thickness at the end of inspiration and TEE is diaphragm thickness at the end of expiration, and it was recorded as a percentage. The speed of diaphragmatic contraction (IS) and relaxation (ES) and the total duration time of the respiratory cycle were recorded (Figure 1).

## RESULTS

### Study population

There were 96 patients enrolled in the study. The median age was 30.0 months (IQR: 10.0–60.0). Forty-eight (50.0%) of the patients were male and 48 patients (50.0%) were female. According to the PRESS classification, 7 (7.3%) patients were grade 0, 16 (16.7%) grade 2, 28 (29.2%) grade 3, 28 (29.2%) grade 4, and 4 (4.2%) grade 5. Three patients required high-flow nasal cannula oxygen (HFNC) and 1 patient required bilevel positive airway pressure (BiPAP) therapy. The median length of stay in the pediatric emergency department was 20.0 hours (IQR: 12.0–34.5). Seventeen patients (17.7%) were admitted to the ward and the median length of stay in the ward was 22.0 hours (11.5–45.0). Finally, total length of stay in

the hospital was 67.0 hours (IQR: 43.0–101.0).

## Ultrasound findings

The LUS findings of our patients were as follows: subpleural consolidation in 70 (72.8%) patients, confluent B-lines in 19 (19.8%) patients, focal multiple B-lines in 4 (4.1%) patients, and pleural effusion in 3 (3.1%) patients. Table 1 shows the M-mode sonographic findings of diaphragm thickness, TF, diaphragm excursion, IS, ES, and total duration time of the respiratory cycle of the patients enrolled in the study. Values of IS and ES were found to have significant positive correlations with respiratory rate and length of stay in hospital and negative correlations with SpO<sub>2</sub> levels evaluated at the time of admission to the emergency department. (Table 2). Additionally, TF values were negatively correlated with respiratory rate ( $p : 0.022$ ,  $r : -0.236$ ) and length of stay in the emergency department ( $p : 0.016$ ,  $r : -0.256$ ).

In order to obtain homogeneous numbers of patients in the clinical severity groups, patients in the groups of PRESS grades 0–1 and grades 4–5 were merged, so four groups were evaluated for clinical severity scores as follows: PRESS scores 0–1, 2, 3, and 4–5. The IS and ES values differed significantly between these four groups; patients with higher clinical scores had increased IS and ES values ( $p < 0.001$ ) (Graphic 1). There was a positive correlation between the clinical score and IS ( $p < 0.01$ ,  $r : 0.541$ ) and ES ( $p < 0.01$ ,  $r : 0.429$ ). Thickening fraction values were also significantly different between groups; patients with higher clinical scores had lower TF values ( $p : 0.001$ ) (Table 3, Graphic 2), and there was a negative correlation between TF and clinical score ( $p < 0.01$ ,  $r : -0.318$ ). Although there was no statistically significant difference, diaphragm excursion was higher in the severe group (PRESS 4–5) than the mild and moderate (PRESS 0–3) group ( $2.2 \pm 0.56$  vs.  $2.2 \pm 0.59$ ). Patients who required respiratory support (HFNC or BiPAP therapy) had higher IS and ES measurements ( $p : 0.001$ ,  $p : 0.004$ ).

Analysis of ROC curves was performed and the value of the area under the curve (AUC) for IS among patients of PRESS grades 4 and 5 was found to be 0.805 (95% confidence interval (CI): 0.670–0.910). At a cut-off level of 0.277 cm/s, the sensitivity and specificity of IS values for PRESS grades 4 and 5 were 87.5% and 51.9%. For ES, the AUC value among patients of PRESS grades 4 and 5 was 0.761 (95% CI: 0.650–0.890). At a cut-off level of 0.248 cm/s, the sensitivity and specificity of ES values for PRESS grades 4 and 5 were 87.5% and 58.2%, respectively (Figure 2).

## DISCUSSION

Recently, point-of-care LUS has been used with growing interest in emergency settings. In a review, ultrasound was defined as the “visual stethoscope” of the 21<sup>st</sup> century <sup>20</sup>. Diaphragm ultrasound is also easy to learn and perform, and the assessments take a short time. It seems that DUS can be easily carried out while performing LUS in the emergency department. Diaphragm ultrasound provides objective, measurable parameters to the clinician, as clinical evaluation or treatment strategies are mostly performed based on subjective clinical findings and thus reflect individual variability. For this reason, in a crowded emergency setting, DUS helps the clinician obtain more objective, reliable, and measurable data. To our knowledge, this is the first study evaluating diaphragm parameters with ultrasound in previously healthy children with pneumonia.

To date, most of the studies about DUS have been performed in adults <sup>15, 21–24</sup>. There are few such studies in children, and in those studies, diaphragmatic dysfunction was evaluated mostly in intensive care units. Diaphragm parameters were obtained to predict diaphragmatic fatigue after cardiac surgery or successful weaning from mechanic ventilation <sup>25–27</sup>. Diaphragm thickness and TF were found to be important predictors of extubation success from mechanic ventilators; TF of  $< 17\%$  was associated with weaning failure. In a few studies, normal values of diaphragm parameters in healthy infants/children were also evaluated <sup>28–29</sup>. None of these studies evaluated all of the parameters that we used to assess diaphragm function. There is one study about previously healthy infants with bronchiolitis aged 1–12 months, evaluating ultrasonographic examinations of the diaphragm to predict the severity of respiratory distress and outcomes <sup>30</sup>. To our knowledge, this is the first study measuring ES with DUS in addition to these parameters.

El-Halaby et al. <sup>28</sup> evaluated the measurements of diaphragmatic excursion and thickness in healthy infants and children. They divided patients into 4 groups according to age and obtained measurements. Correlating our findings with theirs, both diaphragmatic excursion and thickness values were lower than those of even the youngest age group, suggesting that pneumonia causes diaphragmatic dysfunction. Moreover, TF values were associated with the severity of the pneumonia, indicating that diaphragm contractility decreases as the disease severity progresses. Inspiratory slope and ES values were also correlated with PRESS scores, suggesting that inspiratory and expiratory efforts were increased in cases of severe pneumonia. Length of stay in the hospital was correlated with IS and ES as a practical predictor for outcome. Buonsenso et al. <sup>30</sup> found that severe bronchiolitis patients had lower TF than in moderate or mild cases, but there was no statistically significant difference. Thickening fraction was found to have a correlation with SpO<sub>2</sub> at first evaluation in bronchiolitis patients. Diaphragm excursion was lower in patients with moderate eco scores than in those with mild or normal scores, but there was no statistically significant difference between mild and normal eco scores. They concluded that IS measurements were higher in patients who required respiratory support for bronchiolitis, consistent with our study. Additionally, we found that IS and ES values were both associated with the need for respiratory support, signaling that higher inspiratory and expiratory efforts would predict worsening outcomes. In our study, it was shown that there were significant positive correlations between both IS and ES and respiratory rate, while they had negative correlations with SpO<sub>2</sub> levels evaluated at the time of admission to the emergency department. Furthermore, TF values were negatively correlated with respiratory rate. Interestingly, there was no difference between PRESS groups according to diaphragm excursion measurements. This discrepancy may be due to the different pathological features of the two diseases, namely bronchiolitis and pneumonia, respectively.

Our study has some limitations. First, the number of patients was not high enough to establish groups according to age and weight and compare the DUS parameters between them according to severity scores. Nevertheless, diaphragmatic excursion and thickness measurements were lower than those of the youngest healthy age group recorded in another study (30), suggesting that pneumonia does cause diaphragmatic dysfunction. Second, we did not obtain DUS results after recovery, so differences in measurements in the healthy and sick periods were not evaluated.

In conclusion, DUS may be a promising and useful tool to assess diaphragmatic dysfunction in patients diagnosed with pneumonia. Diaphragm parameters, especially TF, IS, and ES, may provide objective and reliable information to predict the severity of the illness, the need for respiratory support, and outcomes. Nevertheless, studies with larger case series are required to reveal the benefits of diaphragm ultrasound in children with different diagnoses.

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