Point of care diaphragm ultrasound in acute bronchiolitis: a measurable tool to predict the clinical, sonographic severity of the disease and outcomes

Nihan Şık[1], Hale Çitlenbik[1], Ali Öztürk[1], Durgül Yılmaz[1], and Murat Duman[1]

[1]Dokuz Eylul University Faculty of Medicine

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Abstract

Background: The aim of this study was to evaluate diaphragmatic parameters in bronchiolitis patients and identify correlations between clinical and sonographic severity scores and outcomes in order to develop a more objective and useful tool in the emergency department. Methods: Children aged between 1 and 24 months and diagnosed with acute bronchiolitis were included in the study. The Modified Respiratory Distress Assessment Instrument (mRDAI) score was used to quantify the clinical severity of the disease. Lung ultrasound was performed and a bronchiolitis ultrasound score (BUS) was calculated. Diaphragm ultrasound was then performed and diaphragm thickness at the end of inspiration and expiration, thickening fraction, diaphragm excursion (EXC), inspiratory slope (IS), expiratory slope (ES), and total duration time of the respiratory cycle were measured. Results: There were 104 patients evaluated in this study. The mRDAI score and BUS had a significant positive correlation. There was a positive correlation between IS and respiratory rate at admission. As the clinical score increased, IS, ES, and EXC measurements rose and they were positively correlated. Values of IS, ES, and EXC were higher in the moderate-severe group than the mild group for both mRDAI and BUS scores. Inspiratory slope values were correlated with the length of stay in the hospital. Conclusion: Values of IS and ES were correlated with clinical and sonographic severity scores. Moreover, IS was a good predictor of outcome. Diaphragm ultrasound appears to be an objective and useful tool to help the physician make decisions regarding the evaluation and management of bronchiolitis.

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Nihan Şık, MD[1], Hale Çitlenbik, MD[1], Ali Öztürk, MD[1], Durgül Yılmaz, Prof.[1], Murat Duman, Prof.[1]

[1] Division of Pediatric Emergency Care, Department of Pediatrics, Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey.

Corresponding author: Prof. Dr. Murat Duman, Division of Pediatric Emergency Care, Department of Pediatrics, Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey. e-mail:mduman@deu.edu.tr, Tel:+902324126015

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Declaration of Conflicting of Interests

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Running head: Diaphragm ultrasound parameters in children with acute bronchiolitis

INTRODUCTION

Acute bronchiolitis (AB) is a viral inflammation of the lower respiratory tract in children younger than 24 months, constituting an important economic and healthcare burden. It is the most common infection of infants requiring hospital admission. Although it usually presents with a benign course, progression to severe illness requiring respiratory support and admission to an intensive care unit unfortunately occurs rapidly in some cases. For this reason, AB is associated with notable morbidity and mortality worldwide.

Diagnosis is based on clinical evaluation and the routine use of laboratory or chest X-ray (CXR) is not recommended because of unnecessary antibiotic overuse [1]. In order to quantify the severity of the disease, clinical severity scores were developed and are widely used to assess the course of the disease and treatment strategy, but they are all based on the subjective clinical assessment of the physician [2].

Point-of-care lung ultrasound (LUS) has been used with growing enthusiasm in pediatric emergency departments recently. It is practical, inexpensive, reproducible, and easy to learn and it seems to be the "visual stethoscope" of the 21st century [3]-5. Transient tachypnea of the newborn, respiratory distress syndrome, pneumonia, pulmonary edema, pneumothorax, and bronchiolitis are some diseases and anomalies that can be assessed using LUS 6-8. Subpleural lung consolidations, confluent B-lines, and pleural line abnormalities were evaluated to be specific ultrasound signs of AB, and the extent of the lesions detected by LUS was associated with the severity of the disease (9). Moreover, LUS was found to be superior to CXR in studies that assessed bronchiolitis patients [1]0-[12]. All these advantages quantify LUS as a useful assessment device, especially for pediatric emergency settings. A bronchiolitis ultrasound score (BUS) was also developed to predict the severity of illness [1]0. It was found to have agreement with clinical severity scores, but performing LUS for bilateral anterior and posterior chest areas and then calculating the score can be difficult and time-consuming. Meanwhile, the infant may not stay calm through the whole period of sonographic assessment. For this reason, a rapid, practical, reliable, and more objective severity score is needed to evaluate patients in the emergency department.

Noninvasive evaluation of the diaphragm by using ultrasonography has gained popularity in both adult and pediatric intensive care units recently. The diaphragm is the main respiratory muscle and diaphragmatic dysfunction may be underdiagnosed because of nonspecific features such as weaning failure from mechanical ventilator, unexplained respiratory distress, lung collapse, or paradoxical abdominal movement during respiration. In the pediatric population, there are few studies evaluating diaphragm parameters to predict extubation success from mechanic ventilation, diaphragmatic fatigue after cardiac surgery, or normal values of diaphragm parameters in healthy children, and only one study has addressed this issue in bronchiolitis patients [11]-[21]. Thus, the aim of this study was to evaluate diaphragmatic parameters in previously healthy bronchiolitis patients and identify correlations between clinical and ultrasonographic severity scores and outcomes in order to develop a more objective and useful tool for use in the emergency department.

MATERIALS AND METHODS

Study Design

After obtaining approval from the Ethics Committee of the Dokuz Eylul University Faculty of Medicine, we performed a prospective study between December 2018 and May 2019. Written informed consent was received from the parents or legal guardians of patients before enrollment. The study was conducted in the Dokuz Eylul University Pediatric Emergency Department. Previously healthy children aged between 1 and 24 months and diagnosed with AB according to the guidelines of the American Academy of Pediatrics were included in the study. The following patients were excluded: those requiring immediate intervention with life-threatening disease, patients with a history of recurrent wheezing (more than 3 attacks) or one major criterion or two minor criteria according to the Modified Asthma Predictive Index, and those with

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chronic respiratory disease, cardiac or neuromuscular diseases, genetic disorders, chest wall abnormalities, prematurity (<34 gestational week), or a history of cardiac or thoracic surgery [22]. The demographic and clinical data were recorded and the patients were grouped to quantify the severity of AB using the Modified Respiratory Distress Assessment Instrument (mRDAI) score, a scale that consists of respiratory rate, use of accessory muscles, auscultation findings, and color, with each parameter scored from 0 to 3 and the total score being categorized as mild (0-4 points), moderate (5-8 points), or severe (9-12 points) for bronchiolitis patients [23]. Vital signs were monitored by a nurse and the patients were evaluated by a pediatric assistant and a pediatric emergency fellow.

Sonographic examination was performed with a Philips ClearVue 350 portable system with an L12-4 MHz linear transducer by a single pediatric emergency fellow who was well trained on LUS for over 2 years. Sonographic examinations were obtained when the participants seemed calm, using pacifiers or distracting their attention somehow during the examination. If they were uncooperative, we waited until they looked calm or fell asleep. Lung ultrasound was performed following a process reported previously [2]4. Both longitudinal and transverse sections were obtained for the anterior, posterior, and lateral chest wall and the BUS was calculated using the methodology described by Basile et al. [1]0 based on the extent of lung involvement (Figure 1). Echographic findings of bronchiolitis were examined for anterior and paravertebral/posterior areas of the thorax and each parameter was scored with 0 to 2 points. The total score was assessed as 0 point: normal lung ultrasound pattern; 1-3 points: mild bronchiolitis, 4-6 points: moderate bronchiolitis; or 7-8 points: severe bronchiolitis [1]0.

The right hemidiaphragm was examined for sonographic evaluation as previous studies detected that there was no difference between the measurements of right and left sides [2]5-[2]7. The transducer was located on the midaxillary or midclavicular line, between the 9th and 10th intercostal areas in the coronal plane and directed medially, cephalad, and dorsally to achieve the best image. The two-dimensional mode was used to identify the diaphragm and M-mode was then used to measure the thickness and display diaphragmatic movement. The diaphragm was imaged as an echogenic line moving freely during inspiration and expiration in M-mode. Inspiration was detected as upward and expiration as downward flexion on the sonographic tracing. The thickness of the diaphragm was measured by the vertical distance between the midpoints of the pleural and peritoneal layers at the end of inspiration and expiration. The thickening fraction (TF) 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. Diaphragm excursion (EXC) was measured as the vertical distance tracing from the baseline to the point of maximum height of inspiration. Inspiratory slope (IS), or the speed of diaphragmatic contraction, and expiratory slope (ES), or the speed of relaxation, were calculated together with the total duration time of the respiratory cycle (Figure 2). Three consecutive respiratory cycles were recorded and the averages of 3 cycles were calculated for each parameter [1]8.

The primary outcome of our study was to determine DUS parameters in bronchiolitis patients and the secondary outcome was to identify the correlations between DUS parameters and clinical and sonographic severity scores, need for respiratory support, and outcomes.

Statistical analysis

All data were analyzed using IBM SPSS software version 22.0 for Windows and a p value of less than 0.05 was considered statistically significant. Data were reported as means with standard deviations (SDs) or medians with interquartile ranges (IQRs). The Mann-Whitney U test was used to compare non-parametric variables. For parametric data, Student's t test was used. Correlations between ultrasound parameters and clinical/echographic scores were assessed with Spearman's rank correlation coefficient.

RESULTS

Study population

One hundred four patients were eligible for the study. The median age was 6.5 months (IQR: 4.0-10.0).

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Sixty-nine (66.3%) of the patients were male and 35 (33.7%) were female. According to the mRDAI scoring, 71 (68.3%) patients were in the mild group (mRDAI score: 0-4), 27 (26.0%) in the moderate group (mRDAI score: 5-8), and 6 (5.7%) in the severe group (mRDAI score: 9-12). When the patients were classified by BUS, 55 (52.9%) patients were in the mild group (BUS: 1-3), 46 (44.2%) were in the moderate group (BUS: 4-6), and 3 (2.9%) were in the severe group (BUS: 7-8). All 6 patients in the severe mRDAI group required high-flow nasal cannula (HFNC) oxygen therapy within two hours after admission. The median length of stay in the pediatric emergency department was 26 hours (IQR: 12.0-48.0). Ten patients (10.3%) were admitted to the ward and the median length of stay in the ward was 143 hours (IQR: 100.0-191.0). The median length of total stay in the hospital was 27 hours (IQR: 12.0-54.0) (min: 4, max: 291 hours).

Ultrasound findings

The M-mode sonographic findings of diaphragm thickness, TF, EXC, IS, ES, and total duration time of the respiratory cycle of the patients enrolled in this study are shown in Table 1. The mRDAI scores and BUS values had a significant positive correlation ($p < 0.001$, $r : 0.760$). There was a positive correlation between IS and respiratory rate at admission ($p < 0.001$, $r : 0.637$). As the clinical score increased, IS ($p < 0.001$,$r : 0.775$), ES ($p < 0.001$, r: 0.444), and EXC ($p < 0.001$, $r : 0.200$) measurements rose and these were positively correlated (Table 2). Additionally, BUS values had a correlation with both IS ($p < 0.001$, $r : 0.562$) and ES ($p : 0.012$, $r : 0.244$) values. Because there were few patients in the severe group according to mRDAI and BUS values, we divided the patients into two groups for comparison as the mild and moderate-severe groups. According to this classification, there were 71 (68.3%) patients in the mild and 27 (31.7%) patients in the moderate-severe group for mRDAI scores and there were 55 (52.9%) patients in the mild and 49 (47.1%) patients in the moderate-severe group for BUS values. Furthermore, values of IS, ES, EXC, and total duration time of the respiratory cycle were also higher in the moderate-severe group than the mild group for both mRDAI scores (for IS and ES: $p < 0.001$; for EXC: $p : 0.003$; for total duration: $p : 0.014$) and BUS values (for IS: $p < 0.001$; for ES: $p : 0.014$; for EXC: $p : 0.036$). Patients who received HFNC oxygen therapy had higher IS ($p : 0.028$) and TEE ($p : 0.023$) measurements and, although not statistically significant, higher EXC values ($p : 0.053$). We could repeat the measurements of diaphragm parameters for 2 patients in 2 hours after starting HFNC oxygen therapy; although we did not have enough patients to statistically evaluate this, we observed that IS, ES, EXC, TEI, and TEE were all decreased as the respiratory support reduced the work of breathing. Values of IS were correlated with both the length of stay in the emergency department ($p : 0.002$, $r : 0.316$) and the total stay in the hospital ($p < 0.001$, $r : 0.492$).

DISCUSSION

Point-of-care LUS has gained significant popularity in emergency settings recently. The earliest studies emphasized that LUS was a valuable tool to identify bronchiolitis and it reduced the need for CXR. Moreover, LUS was in agreement with clinical scores to predict the severity of the disease. Lung ultrasound was found to be an accurate device for both diagnosis and management in emergency departments [3-5, 10-12]. We have reported that sonographic scores had significant agreement with clinical scores to predict the disease severity and the need for respiratory support, consistent with previous studies. However, clinical scores may vary individually as non-objective parameters. Performing LUS for bilateral anterior and posterior chest areas to obtain echographic scores may be difficult and time-consuming as infants may not stay calm during the whole period of assessment. For this reason, these scoring tools may not be rapid, practical, or objective enough to accurately quantify the severity of the disease and guide management in the emergency department.

Diaphragm ultrasound (DUS) has also been used in adult and pediatric intensive care units in order to identify weaning success from mechanical ventilator, diaphragm paralysis after cardiac/thoracic operations, or normal values for healthy individuals. In these studies, TF, EXC, and TEE were found to be good predictors for successful weaning or diaphragmatic fatigue in particular [15-17]. There are few such studies involving the pediatric population, unfortunately.

To our knowledge, there is one study evaluating DUS parameters in infants with bronchiolitis. Buonsenso et

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al. [21] concluded that clinical score was correlated with echographic score. The IS values differed significantly between echographic score groups and patients needing respiratory support had higher IS values, supporting our findings. They also reported that EXC was lower in the moderate echographic group compared with the mild group, but there was no statistically significant difference between the mild and normal group. In our study, IS, ES, and EXC values were higher in the moderate-severe group than the mild group for both clinical and echographic scores. Because there were no patients with normal echographic scores, we could not compare that category. Buonsenso et al. [21] did not conclude any correlation between respiratory rate and diaphragm parameters, although we found IS to have a significant correlation with respiratory rate at admission. This discrepancy may be related to the different numbers of patients in the two studies (61 versus 104). Although TF was found to be a valuable predictor for extubation success from mechanical ventilator in previous studies, it did not differ between bronchiolitis severity groups in either of these studies. Buonsenso et al. [21] also concluded that patients with lower TF values required respiratory support, in contrast to our findings, wherein we considered IS and TEE for predicting the need for respiratory support. In their study, 25 of 61 patients required respiratory support, 5 of whom were in the mild group, 15 in the moderate group, and 5 in the severe group, although all 6 patients who received HFNC oxygen therapy were in the severe group. Measurements were evaluated at admission in both studies. We could repeat the measurement of diaphragm parameters of 2 patients in 2 hours after starting HFNC oxygen therapy; IS, ES, EXC, TEI, and TEE were all decreased as the respiratory support reduced the work of breathing, but this difference was not observed for TF. The number of patients for this observation is too low for a firm conclusion, but this may have been related to the pathophysiology of bronchiolitis. El-Mogy et al. [2]8 concluded that diaphragm thickness increased and excursion decreased at higher levels of continuous positive airway pressure (CPAP), although there were no significant differences found among diaphragmatic dimensions for levels of either nasal CPAP or high-flow therapy. To our knowledge, there is no study evaluating the effects of HFNC oxygen therapy on DUS parameters among children. In comparison with a study that evaluated normal TEE and EXC measurements in healthy children, our measurements were lower than those among the age group of 1-12 months, suggesting that bronchiolitis causes diaphragmatic dysfunction. Nevertheless, our EXC measurements were also lower than those in a study that evaluated bronchiolitis patients [21]. We think that measurement in a semi-recumbent or supine position could change EXC values. In an adult study aiming to show changes in diaphragmatic function during breathing control in healthy participants, EXC values before the test were similar to our findings. Diaphragm excursion measurements differed in various studies, interestingly [1]9´[2]9.

Our study has some limitations. First, there were few patients in the severe bronchiolitis group according to both mRDAI and BUS values, so we had to compare diaphragm parameters between mild and moderate-severe groups. Second, we could only repeat the examination of DUS after starting HFNC oxygen therapy for 2 of 6 patients; if we had been able to perform the examination for all 6 patients, we could have obtained more useful information.

In conclusion, there was agreement between the clinical and sonographic severity scores, so lung ultrasound was considered valuable for the evaluation of bronchiolitis. To our knowledge, this is the first study evaluating ES measurements with DUS in bronchiolitis patients. To determine the severity of the disease, IS and ES measurements were both qualified as reliable predictors. Additionally, IS values provided convenient information about the length of stay in the hospital. Diaphragm ultrasound appears to be an objective and useful tool to help the physician make decisions about the evaluation and management of bronchiolitis in emergency settings.

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