Diaphragm Ultrasonography to Predict Noninvasive Respiratory Treatment Failure in Infants With Severe Bronchiolitis

Ana Gómez-Zamora, Diego Rodriguez-Álvarez, Iria Durán-Lorenzo, Cristina Schüffelmann, Miguel Rodríguez-Rubio, and Paloma Dorao Martinez-Romillo

BACKGROUND: Noninvasive respiratory support is commonly used in treatment of bronchiolitis. Determinants of failure are needed to prevent delayed intubation. METHODS: We conducted a prospective observational pilot study in infants admitted to a pediatric ICU. Diaphragmatic excursion (dExc), diaphragmatic inspiratory/expiratory time, and diaphragmatic thickening fraction (dTF) were recorded at admission, 24 h, and 48 h in both hemidiaphragms. RESULTS: Twenty-six subjects were included (14 on HFNC and 12 on NIV) with a total of 56 ultrasonographic evaluations. Three subjects required invasive ventilation. Sixty-four percent of the subjects on HFNC required NIV as rescue therapy and 2/14 invasive ventilation (14.2%). In the HFNC group there were no differences in dExc between those who required escalation to NIV or invasive ventilation and those who didn't. Left dTF was higher in subjects on HFNC requiring invasive ventilation versus those needing NIV (left dTF 47% vs 22% [13–30]; *P* = .046, r = 0.7). Diaphragmatic I:E ratios were higher in infants on HFNC requiring invasive ventilation and diaphragmatic expiratory time was shorter (left *P* = .038; right *P* = .02). In the NIV group there were no differences in dExc, I:E ratios, or dTF between subjects needing escalation to invasive ventilation and those who didn't. We found no correlation between a clinical work of breathing score and echographic dTF. CONCLUSIONS: In infants with moderate or severe bronchiolitis receiving HFNC, the use of ultrasonographic left dTF could help predict respiratory treatment failure and need for invasive ventilation. The use of ultrasonographic dExc is of little help to predict both. *Key words: diaphragm; noninvasive ventilation; mechanical ventilation; ultrasonographic imaging; POCUS; bronchiolitis; viral; pediatric intensive care unit.* [Respir Care 2022;67(4):455–463. © 2022 Daedalus Enterprises]

Introduction

Acute bronchiolitis is a leading cause of hospitalization among infants worldwide, with pediatric ICU (PICU) admission rates of 9–13% in hospitalized and previously healthy infants and 36% in those with comorbid conditions. Among infants admitted to a PICU, about 2–5% will require invasive mechanical ventilation, with a mortality rate of 1%.[1-3] Supportive treatment, noninvasive respiratory support, and, when needed, invasive mechanical ventilation remain the standard of care in infants with severe bronchiolitis admitted to a PICU.

Predictive factors for PICU admission have been described in the literature.[3,4] In an attempt to increase the performance of clinical scores, some authors have advocated for the inclusion of point-of-care lung parenchyma ultrasound in the evaluation of infants with bronchiolitis.[5-10] Nevertheless, the clinical assessment of the effort of breathing (EOB) is limited by subjectivity and poor specificity; and it is based on clinical experience, failing by itself to predict clinical outcomes.[11-15] Objective measurements of EOB in critically ill children could be more accurate but may be limited for routine clinical care because of their invasiveness, cost, required technical expertise, and necessary equipment.[16]

Point-of-care ultrasound (POCUS) of the diaphragm allows for the quantification of diaphragmatic contractile activity in real time by measuring the diaphragmatic excursion (dExc), thickness, and thickening fraction (dTF).[17,18] Ultrasonographic assessment of the dTF has been described as a good indicator of changes in inspiratory muscle effort and work of breathing in adults.[19-21]

The primary aim of this pilot study was to describe the ultrasonographic indices of diaphragmatic contractile activity in infants with moderate and severe bronchiolitis supported with high-flow nasal cannula (HFNC) or noninvasive ventilation (NIV) and their need for invasive ventilation. Secondary objectives were to describe these measures according to the radiological findings, clinical scores, and outcomes.

QUICK LOOK

Current knowledge

Ultrasonographic measurements (diaphragm thickening fraction, amplitude of diaphragm movement) in infants with acute bronchiolitis are correlated with outcome.

What this paper contributes to our knowledge

In this prospective study, we evaluate the usefulness of ultrasonographic indices of diaphragmatic contractile activity in infants with severe bronchiolitis admitted to pediatric ICU in predicting respiratory treatment failure and the need of invasive mechanical ventilation. Infants on high-flow nasal cannula who required escalation to invasive ventilation had greater diaphragmatic thickening, shorter expiratory times, and higher breathing frequency.

Methods

We conducted a prospective observational pilot study in the PICU of a public, university-affiliated hospital in Madrid, Spain, from October 2018–March 2019. The study setting was a 16-bed medical-surgical PICU with approximately 1,000 admissions per year. The institutional ethics committee approved the study (reference number PI-3478). Fully written informed consent was obtained from the parents or legal guardians of the participants before inclusion.

Subjects and Study Protocol

Infants (< 6 month old and > 3 kg of weight) with moderate and severe bronchiolitis (Wood Downes-Ferres scale > 6) admitted to the PICU were enrolled. In compliance with the standard operating procedure of our department, the subjects were placed on HFNC (Airvo 2, Fisher & Paykel, Auckland, New Zealand) (air flow 2 L/kg/min; with F_{IO_2} titrated to a minimal S_{pO_2} 90%) or NIV (Servo-i, Maquet, Rastatt, Germany; with a total face mask PerforMax XXS or XS Respironics; Philips, Murrysville, Pennsylvania). Treatment failure was defined according to institutional protocols (Supplementary Table 1, see related supplementary materials at http://www.rc.rcjournal.com). Clinical variables, HFNC, or ventilator settings and ultrasound examination were collected at admission, 24 h, and 48 h of PICU admission. Subjects on NIV received oral sedation with clonidine (3–5 μg/kg/dose each 6 h) or continuous intravenous perfusion of dexmedetomidine (0.4–0.7 μg/kg/h) if a second vascular access was available, according to our institutional PICU sedation protocol. We registered the Richmond Agitation-Sedation Scale (RASS) in the study protocol. Subjects were in a semi-recumbent position throughout the study (head of bed elevated to 30°). Patients who weighed < 3 kg, who were in a palliative situation, who had oncologic diseases, hemodynamic instability, vomiting, pneumothorax, or with a tracheostomy in place were excluded.

Ultrasonographic Measurements

Ultrasonography was performed by 2 trained operators (AGZ and DRA) using a LOGIQ F6 device (GE Healthcare, Madison, Wisconsin) equipped with a high-resolution (6–13 MHz) linear probe and 3–5 MHz convex phased-array probe. POCUS of both hemidiaphragms (right [R] and left [L]) was performed at admission, 24 h, and 48 h of PICU admission. The dExc, speed of diaphragmatic contraction, diaphragmatic inspiratory time (dT_I), diaphragmatic expiratory time (dT_E), as well as the dTF (dTF = [end-inspiratory thickness − end-expiratory thickness) / end-expiratory thickness * 100]) were measured.

Images were obtained as previously described,[17,18] with a phased-array transducer (3–5 MHz). M-mode was then used to calculate dExc, diaphragm movement toward the transducer (positive deflection on M-mode) or away from the transducer (negative deflection on M-mode), the speed of the diaphragmatic contraction, and dT_I and dT_E (Fig. 1). Measurements of 3 consecutive breaths were performed by

Drs Gómez-Zamora, Rodriguez-Álvarez, Schüffelmann, Rodríguez-Rubio, and Martinez-Romillo are affiliated with Pediatric Intensive Care Department, Hospital Universitario La Paz, Madrid, Spain. Dr Durán-Lorenzo is affiliated with Pediatric Department, Hospital Fundación Jiménez Díaz, Madrid, Spain.

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The study was performed at Pediatric Intensive Care Department, Hospital Universitario La Paz, Madrid, Spain.

Supplementary material related to this paper is available at http://rc.rcjournal.com.

Correspondence: Ana Gómez-Zamora MD, Pediatric Intensive Care Department, Hospital Universitario La Paz, Paseo de la Castellana 261, 28046, Madrid, Spain. E-mail: agomezz@salud.madrid.org.

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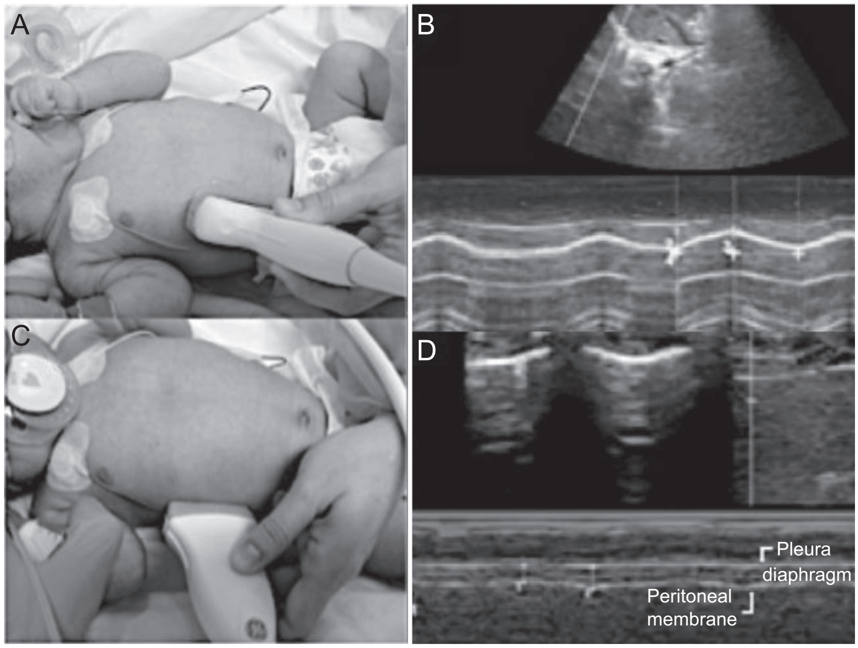

Fig. 1. Diaphragmatic excursion measure with a phased-array transducer (3–5 MHz) (A, B) and diaphragmatic thickening fraction obtained at the zone of apposition of the diaphragm to the rib cage, with a high-frequency linear-array probe (6–13 MHz) (C, D).

the same operator while the second operator reviewed the recorded images and collected them in a database.

DTF assessments were obtained at the zone of apposition of the diaphragm to the rib cage, with a high-frequency linear-array probe (6–13 MHz). The ultrasonographic appearance of the diaphragm in the zone of apposition is seen as a 3-layered structure composed of 2 parallel echogenic layers of diaphragmatic pleura and peritoneal membranes and between them a non-echogenic layer of muscle (Fig. 1). Three subsequent inspiratory and expiratory measures of the non-echogenic layer of muscle (peritoneal and pleural membranes were not included) were averaged. The dTF was calculated using the M-mode in the zone of apposition (Fig. 1).

Statistical Analysis

Data were analyzed using SPSS 24.0 toolbox (version 24; IBM, Armonk New York). Normal goodness of fit was evaluated using the Shapiro-Wilk test. The nonparametric data are expressed as median and interquartile range (IQR 25–75%) or the interquartile range in the case that the group only has 2 measures. For the nonparametric contrast of 2 unrelated samples, the Mann-Whitney U test was used. The Spearman (nonparametric data) test was used for correlation analysis between variables. To analyze the association among qualitative variables, the chi-square test was used. Statistical significance was set at $P < .05$.

We based our sample size calculation on the measurements reported by Bounsenso et al,[9] namely end expiratory thickness 2.19 $\pm$ 0.62 mm, end inspiratory thickness 3.17 $\pm$ 0.72 mm, and dExc 10.38 $\pm$ 4.00 mm. We used a confidence interval width probability of 0.9. We hypothesized an absolute error in the estimation of the means of 0.6 mm for the end-expiratory thickness, 7 mm for the end-inspiratory thickness, and 4 mm for the dExc. We obtained the following sample sizes for each measure: 26, 25, and 24 infants. The largest sample size (26 infants) was used to carry out the study.

Results

Study Sample

Between October 2018–March 2019, a total of 90 infants met inclusion criteria; 26 of them consented to participate and were recruited. The rest of the infants were not recruited because of technical and organizational issues (lack of diaphragmatic ultrasound training or lack of research personnel).

Respiratory syncytial virus was the main etiological agent in 24 infants (92%). The median length of PICU stay was 4 d (3–6). The initial therapy was HFNC in 14 subjects (54%) and NIV in 12 (46%). Three subjects required orotracheal intubation (11%). The clinical characteristics of the participants and risk factors are described in Table 1. Subjects who required escalation to invasive ventilation had a venous P_{CO_2} of 48 (45–62) mm Hg compared to the group that did not require invasive ventilation: 47 (IQR 45–66) mm Hg. Support with HFNC was 2 L/kg/min flow with F_{IO_2}: 0.40

Table 1. Subject Characteristics Regarding the Need for Invasive Ventilation

	HFNC or NIV $n = 23$	Invasive Ventilation $n = 3$
Age, months	1 (1–2)	2 (1–2)
PICU admission weight, g,	4,300 (3,600–5,000)	3,600 (3,500–4,800)
Gestational age, d	274 (263–280)	241 (210–268)
Male/female, *n*	14/9	2/1
Weight at birth, g	3,200 (2,590–3,550)	2,880 (2,090–2,996)
Breastfeeding	17 (74)	2 (67)
Previous administration of palivizumab	1 (4)	1 (33)
Apneas	5 (22)	1 (33)
Comorbidities	2 (9)	1 (33)
Atopy parents	8 (31)	1 (33)
Smoking parents	3 (13)	1 (33)
Siblings	21 (91)	2 (67)
$PvCO_2$, mm Hg	47 (45–66)	48 (45–62)
F_{IO_2}	0.39 (0.32–0.48)	0.40 (0.40–0.60)

Data are shown as median (IQR) or *n* (%) unless otherwise noted.
HFNC = high-flow nasal cannula
NIV = noninvasive ventilation
PICU = pediatric ICU
$PvCO_2$ = venous partial pressure of carbon dioxide

(0.40–0.60) in the group that required invasive ventilation versus 0.39 (0.32–0.48) in the group who did not.

A total of 56 ultrasonographic evaluations were performed (POCUS of both hemidiaphragms was performed at admission, 24 h, and 48 h of PICU admission). At the time of ultrasonographic evaluation, respiratory support was HFNC in 31 subjects and NIV in 25 subjects. The timeline of ultrasound assessments, respiratory support, and the respiratory evolution of subjects is shown in Figure 2.

Ultrasound Evaluation and Need of Invasive Ventilation

The study sample was analyzed in 2 groups: (1) HNFC group (ie, subjects receiving HFNC support at the time of ultrasound evaluation) and (2) NIV group (ie, subjects receiving NIV at the time of ultrasound evaluation).

The POCUS measurements of both hemidiaphragms in the HFNC group are reported in Table 2 and Figure 3. Ultrasound measurements performed at admission are shown in Supplementary Table 2 (see related supplementary materials at http://www.rc.rcjournal.com). No differences were observed between the subgroup that required escalation to NIV compared to those who remained on HFNC.

Infants on HFNC who required escalation to invasive ventilation had statistically significant higher left dTF, dT_E, and higher breathing frequency.

Regarding the NIV group, the subject requiring orotracheal intubation had a PEEP = 5 cm H_2O, pressure support (PS) = 5, tidal volume (V_T) = 10 mL/kg, F_{IO_2}= 0.4, and P_{CO_2} = 53 mm Hg. The subgroup that did not require invasive ventilation had PEEP = 5 (IQR 5–5) cm H_2O, PS = 5 (IQR 4–5) cm H_2O, F_{IO_2} = 0.4 (IQR 0.30–0.53), V_T = 10 (IQR 10–11) mL/kg, and P_{CO_2} = 55 (IQR 42–63) mm Hg. RASS score was 0 in the infant who required invasive ventilation and 0 (IQR 0–1) in the rest of subjects with NIV who received sedation. No differences were found in dExc, speed of dExc, and echographic dI:E ratios between those who required invasive ventilation and those who didn't. Ultrasonographic left dTF was 67% in the infant on NIV requiring invasive ventilation versus 22% (15–29) in those on NIV who were not intubated, but this result was not statistically significant (Supplementary Table 3, see related supplementary materials at http://www.rc.rcjournal.com).

Radiological Atelectasis and Diaphragm POCUS

At admission, a chest x-ray was performed. Atelectasis was found in 19 subjects (73%). Ten participants had radiological atelectasis on the upper quadrants and 9 on the lower quadrants. Subjects with lower radiologic atelectasis had statistically significant higher left dTF and lower right dExc. The finding of lower-quadrants atelectasis upon admission was statistically correlated with escalation of respiratory support from HFNC to NIV or invasive ventilation (chi-square test = 5.67, P = .02). Table 3 and Figure 4 show the relationship between lower-quadrant radiological atelectasis and ultrasonography parameters.

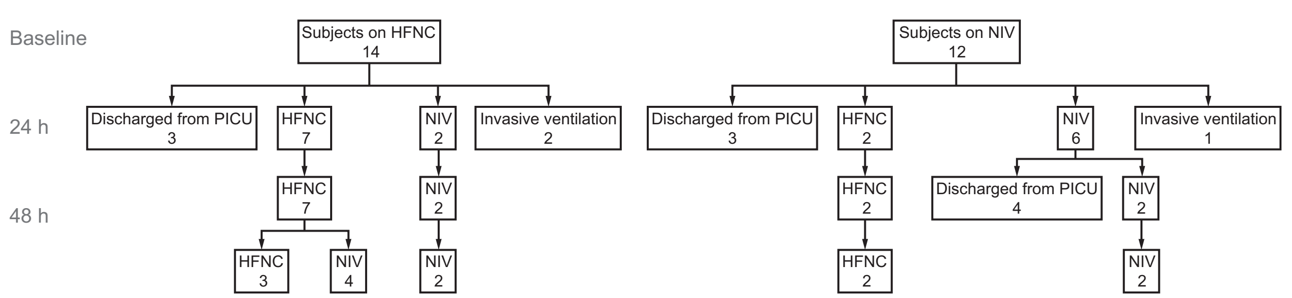

Fig. 2. Flow chart. HFNC = high-flow nasal cannula, NIV = noninvasive ventilation, PICU = pediatric intensive care unit.

Table 2. Diaphragmatic Ultrasound Parameters With HFNC Related to Escalation of Respiratory Support

	HFNC to HFNC[a] $n = 21$	HFNC to NIV[b] $n = 6$	HFNC to Invasive Ventilation[c] $n = 2$	1 vs 2	2 vs 3	1 vs 3
Left dTF %	25 (14–38)	22 (13–30)	46.5 (15)	.60	.046	.13
Right dTF %	20 (14–31)	29 (23–32)	39.5 (35)	.24	.74	.23
Left dExc mm	6.2 (5.3–8.0)	6.2 (5.4–9.0)	6.1 (2.2)	.75	.51	.83
Right dExc mm	5.6 (4.8–7.5)	6.7 (5.6–8.3)	5.2 (1.1)	.22	.18	.55
Left SPcont, cm/s	1.8 (1.2–2.2)	1.7 (1.3–4.0)	1.6 (0.3)	.77	.74	.66
Right SPcont, cm/s	2 (1.2–2.3)	2 (1.2–3.2)	1.1 (0.3)	.56	.18	.08
Left inspiratory time, s	0.41 (0.34–0.55)	0.31 (0.24–0.47)	0.40 (0.05)	.12	.51	.91
Left expiratory time, s	0.67 (0.56–0.76)	0.55 (0.43–0.75)	0.28 (0.09)	.23	.046	.038
Left I:E ratio	0.65 (0.51–0.81)	0.59 (0.49–0.74)	1.48 (0.33)	.68	.046	.038
Right inspiratory time, s	0.43 (0.36–0.47)	0.39 (0.26–0.46)	0.42 (0.13)	.31	.51	.96
Right expiratory time, s	0.60 (0.47–0.72)	0.64 (0.36–0.70)	0.32 (0.26)	.68	.18	.064
Right I:E ratio	0.68 (0.57–0.90)	0.63 (0.56–0.89)	1.44 (0.72)	.86	.10	.02
Breathing frequency, breaths/min	44 (32–52)	34 (31–63)	76 (28)	.76	.14	.032

Data are shown as median (IQR) or *n* (%) unless otherwise noted.
dTF = diaphragm thickening fraction
dExc = excursion of diaphragm
SPcont = speed of contraction of diaphragm
I:E = inspiratory:expiratory
[a] t = 0, 7 measurements;
t = 24 h, 9 measurements
t = 48 h, 5 measurements
[b] t = 0, 2 measurements
t = 24 h, 0 measurements
t = 48 h, 4 measurements
[c] t = 0, 2 measurements
t = 24 h, 0 measurements;
t = 48 h, 0 measurements. Only 2 measurements were made in this group.

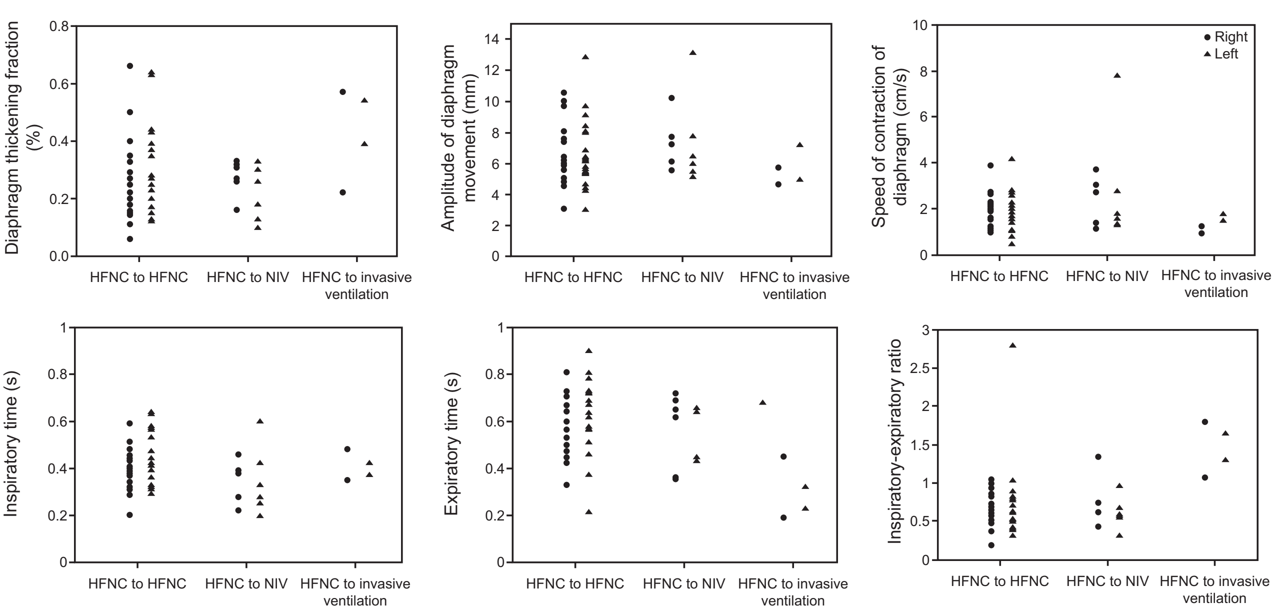

Fig. 3. Echographic measurements (diaphragm thickening fraction, amplitude of diaphragm movement, speed of contraction, inspiratory time, expiratory time, and inspiratory:expiratory ratio) of the left and right diaphragms related to escalation of respiratory support.

Table 3. Ultrasonographic Parameters in the First Ultrasound Depending Related to Radiological Involvement of the Lower Lobes

Lower Lobes Involvement	Yes $n = 9$	No $n = 17$	P
Left dTF %	35 (21–54)	18 (12–27)	.03
Right dTF %	30 (12–35)	25 (17–36)	.85
Left diaphragm excursion, mm	6 (4.2–7.5)	6.9 (4.6–8.9)	.49
Right diaphragm excursion, mm	5.6 (3.5–6.0)	6.4 (5.3–7.7)	.045
Left SPcont, cm/s	1.3 (0.6–2.9)	1.8 (1.6–2.9)	.26
Right SPcont, cm/s	1.4 (1.1–1.9)	1.9 (1.4–3.2)	.12

Data are shown as median (IQR) or n (%) unless otherwise noted.
dTF = diaphragm thickening fraction
SPcont = speed of contraction of diaphragm.

Diaphragm POCUS and Clinical Score

We found no correlation between ultrasound measurements and a clinical score used to evaluate respiratory distress in infants with bronchiolitis (Wood-Downes Clinical Scoring System Modified by Ferres) (Supplementary Tables 4 and 5, see related supplementary materials at http://www.rc.rcjournal.com).

Diaphragm POCUS and PICU Outcomes

There were positive correlations between PICU length of stay (LOS) and the echographic dI:E ratio ($P = .001$, r = 0.843) and a negative correlation between PICU LOS and dT_E ($P = .003$, r = −0.661). The duration of HFNC support was negatively correlated with right dExc ($P = .031$, r = −0.524), whereas NIV support days were correlated with left dTF ($P = .005$, r = 0.534), right dTF ($P = .036$, r = 0.597), left dExc ($P = .030$, r = 0.516), and right dExc ($P = .048$, r = 0.473).

Discussion

The main findings of our study were (1) infants who required invasive ventilation had higher dTF, shorter dT_E, and higher breathing frequency; (2) lower-quadrant atelectasis in admission chest radiograph was associated with diaphragmatic POCUS showing higher dTF and lower dExc and with a higher need for escalation in respiratory support; and (3) diaphragmatic POCUS parameters are correlated with relevant PICU outcomes such as PICU LOS and days of respiratory support.

To our knowledge, this is the first ultrasonographic study assessing diaphragmatic POCUS values in infants with moderate-to-severe bronchiolitis requiring noninvasive respiratory support in a PICU.

Diaphragm POCUS is an evolving, noninvasive technique, and it is accepted as a reliable tool for assessing the diaphragm function in mechanically ventilated patients.[22-27] Ultrasonographic diaphragm thickening has been described as a good index of diaphragmatic efficiency as pressure generator.[20] In adult studies, the right dTF has demonstrated a good correlation with inspiratory muscle effort and objective work of breathing measurements such as esophageal or transdiaphragmatic pressure-time product (PTP) or electrical diaphragmatic activity (EA_{di}).[19-21] We found that in infants with moderate or severe bronchiolitis with noninvasive respiratory support the use of ultrasonographic dTF and diaphragmatic inspiratory time (T_I/T_{tot}) could reflect EOB and could help predict respiratory failure and the need for invasive ventilation.

The feasibility and reproducibility of right hemidiaphragm measurements have been shown to be superior to those of the left hemidiaphragm, and no significant difference in diaphragm thickness and contractility has been noted between the left and right hemidiaphragms in adult patients.[22,23] In our study, we found that left hemidiaphragm ultrasonography,

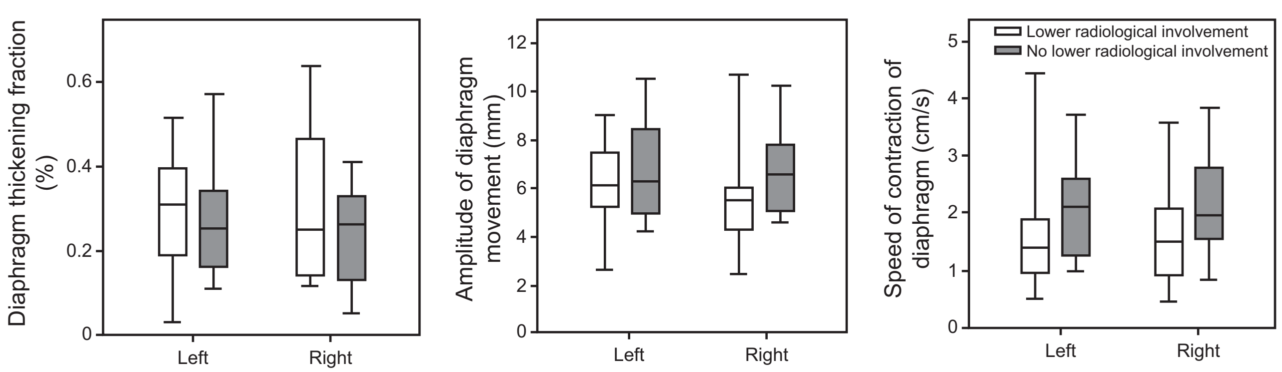

Fig. 4. Box plot graphs show the ultrasonographic diaphragmatic measurements in both diaphragms in children with acute bronchiolitis, depending on whether they have lower radiological involvement or not. The boundary of the box closest to zero indicates the 25th percentile; a line within the box marks the median, and the boundary of the box farthest from zero indicates the 75th percentile. Error bars above and below the box indicate the 90th and 10th percentiles. Lower radiological involvement was associated with diaphragm thickening fraction, amplitude of diaphragm movement, and speed of contraction.

though more difficult to assess, is feasible in infants with the probe positioned in the midaxillary line and the left apposition zone.

Although diaphragmatic dysfunction is a current topic of interest in pediatric critical care, most studies have been conducted in mechanically ventilated children.[28-33] In the PICU population, calculating diaphragmatic thickening is feasible and highly reproducible and is useful to diagnose diaphragm atrophy, which can affect up to 50% of pediatric mechanically ventilated patients[30] and is associated with prolonged NIV following extubation.[31]

DExc and dTF have seldomly been assessed in spontaneously breathing neonates or children.[9,35,36] In 2001, Rehan et al described diaphragmatic dimensions (excursion, thickness, and dTF) in healthy preterm infants who did not show any signs of respiratory distress and were not receiving respiratory support.[35] The values of dTF for healthy preterm infants, with postmenstrual age of 29–31 weeks, were 27 ± 9%.

Although the diaphragm plays a fundamental role, the anatomical configuration of the diaphragm and the chest wall in infants (compliant chest wall and more horizontal insertion of diaphragm to the chest wall) makes the use of accessory inspiratory muscles and an increased breathing frequency necessary to maintain an adequate ventilation in respiratory failure. In our study, we found that subjects on HFNC requiring intubation had a significantly higher breathing frequency, but we found no correlation in those infants requiring escalation to NIV or intubation from NIV. Interestingly, the subjects on HFNC requiring treatment escalation had higher I:E ratios (higher T_I/T_{tot}) that resulted in a reduced dT_E, indicating an impending respiratory failure. Prolongation of inspiratory time offers an energetically advantageous strategy of compensating an increased inspiratory resistive load and may be modulated by behavioral and cortical adaptations. At high inspiratory load close to the fatigue threshold, there is a progressive decrease in V_T, T_I, V_T/T_I, and T_{tot} and an increase in T_I/T_{tot}. When the diaphragm can still compensate, there is an augmentation of the dTF in order to maintain an adequate minute ventilation and adequate functional residual capacity. If the mechanical load (resistive or elastic) is excessive and the diaphragm is unable to compensate, there may be a decrease in V_T or T_I or both.[25,34,37] Our data suggest that dTF could reflect EOB in infants with moderate-severe bronchiolitis with noninvasive respiratory support, since patients requiring intubation and mechanical ventilation have higher dTF. Interestingly, infants with higher T_I/T_{tot} had a longer PICU stay. Because of our small sample size, we were unable to determine a cutoff dTF percentage that could identify infants at high risk of severe respiratory failure.

In our study, the use of ultrasonographic dExc was of little help to predict respiratory failure and the need of escalation of respiratory support, but it was inversely correlated with duration of HFNC support. The mean right dExc in the HFNC group was 5.7 mm (4.9–7.6) and in the NIV group 6.6 mm (4.7–7.9) compared to 6.4 ± 2.1 mm described in healthy children.[36] DExc is associated with inspiratory volume but does not correlate with other indices of respiratory effort. DExc is influenced by the respiratory drive and the respiratory loads imposed by the lung and rib/abdominal cage (eg, ascites, atelectasis) and shouldn't be used as the sole indicator of diaphragmatic strength.[25,37]

Buonsenso et al[9] found that infants with bronchiolitis who needed respiratory support during admission present a higher inspiratory diaphragmatic excursion (mean right dExc was 10.38 ± 4.00 mm) and a decrease in dTF. This difference with our findings could be related to the fact that we performed the ultrasonographic evaluation after initial stabilization in non-strict spontaneous ventilation as our infants were already assisted on HFNC or NIV, both of which reduce the EOB.[38] The amount of continuous positive pressure generated by HFNC at 2 L/Kg/min, despite low, could have affected the dExc, as may have PEEP and pressure support during NIV. In addition, 34.6% of the infants suffering bronchiolitis in our series presented lower basal atelectasis in the chest x-ray that could impair the shape and motion of the diaphragm, limiting also the dExc and speed contraction values and associating an increase dTF as described previously.

We saw no differences in dExc or dTF between subjects on HFNC or NIV despite the fact that NIV should reduce the inspiratory effort and dTF. In adult subjects on invasive mechanical ventilation or NIV, the dTF decreases with increasing levels of PS, representing a reliable indicator of inspiratory muscle effort in response to modifications of the support level.[20] An explanation of our findings could be the fact that during NIV we set a relative low level of PS as the study wasn't designed to assess the dTF variation with PS level modifications.

No correlation was found between the clinical score (Wood-Downes Clinical Scoring System Modified by Ferres) and the need for invasive ventilation in infants supported with HFNC or NIV as previously described[4,12] nor between the clinical score and echographic dTF. Clinical assessments of EOB have been previously shown to correlate with reduced FEV_1 and oxygen saturation in children with asthma.[39,40] In critically ill children, it is unknown if clinical score assessments correlate with objective measures of EOB and with the need for subsequent respiratory support.[16,41] Despite the subjectivity of the clinical assessment scales for infants with bronchiolitis (eg, degree of retractions), an explanation for our result could be that the Wood-Downes Clinical Scoring System Modified by Ferres evaluates several domains (wheezing, breathing frequency, heart rate, retractions, air entry, and cyanosis), whereas the ultrasonographic evaluation of dTF as indicator of EOB evaluates just one of the items assessed by the clinical scale. We found just one study in the literature comparing ultrasound dTF with clinical scores in infants with bronchiolitis.[9] They describe lower dTF in subjects with severe bronchiolitis, indicating incipient diaphragm dysfunction in these infants, though there was no statistically significant difference when comparing between the all clinical score groups, probably due to the low number of patients with severe clinical score.

Our limitations include a small simple size including only 3 intubated subjects, which may limit the generalizability of the data and the lack of a control group without respiratory support. In addition, objective measures of the inspiratory muscle effort (esophageal, diaphragmatic PTP, or EA_{di}) were not used in our study. Additionally, we did not perform lung parenchyma POCUS. Our primary end point was the study of diaphragmatic ultrasound although the assessment of lung aeration could have added more information about prognosis in our series as has been described previously.[5-10] Although Zambon et al[23] show that measurements of the left hemidiaphragm were less feasible (83%), in our infant study we were able to obtain 100% of the measurements of the left hemidiaphragm easily. In the work of Goligher et al,[22] the 95th percentile in the variation of intra-observer repeatability of the left dTF was 13%, whereas the inter-observer reproducibility was 39%. In our study, to reduce this variability, the ultrasound measurements were performed by the same operator during 3 consecutive respiratory cycles, while a second operator performed the average of the measurements and collected them in the database.

Conclusions

We found that in infants with moderate and severe bronchiolitis, the use of ultrasonographic dTF and diaphragmatic T_I/T_{tot} could reflect the EOB and when associated to higher respiratory rate and lower-quadrant atelectasis could help to predict noninvasive respiratory treatment failure and the need of intubation and mechanical ventilation. Diaphragm POCUS may have implications for monitoring and early treatment in infants suffering respiratory distress due to bronchiolitis. Future randomized controlled trials should assess if the use of diaphragm ultrasonography impacts acute and long-term outcomes in this population.

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