



Point-of-care lung ultrasound in infants with bronchiolitis in the pediatric emergency department: a prospective study

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Abstract

Bronchiolitis is the most common cause of hospitalization of children in the first year of life. The lung ultrasound is a new diagnostic tool which is inexpensive, non-invasive, rapid, and easily repeatable. Our prospective study was conducted in the emergency department and all patients underwent a routine clinical evaluation and lung ultrasound by the pediatricians who defined the clinical and the ultrasound score. We enrolled 76 infants (median age 90 days [IQR 62–183], 53.9% males). In nasopharyngeal aspirates, the respiratory syncytial virus was isolated in 33 patients. Considering the clinical score, children with higher score had a higher probability of requiring respiratory support (p 0.001). At the ultrasound evaluation, there was a significant difference on ultrasound score between those who will need respiratory support or not (p 0.003). Infants who needed ventilation with helmet continuous positive airway pressure had a more severe ultrasound score (p 0.028) and clinical score (p 0.004), if compared with those who did not need it.

Conclusion: Our study shows that lung ultrasound in the bronchiolitis may be a useful method to be integrated with the clinical evaluation to better define the prognosis of the individual patient. Multicenter studies on larger populations are necessary to confirm our data.

What is Known:

- Bronchiolitis is the main cause of lower respiratory tract infection in children younger than 24 months.
- Ultrasound can evaluate the lung parenchyma without ionizing radiations.

What is New:

- Lung ultrasound may be a useful diagnostic tool to define the prognosis of the infants affected by bronchiolitis if performed at the first assessment in the emergency department.
- The score obtained at the ultrasound evaluation is higher in those who will need oxygen therapy during admission for more time and in those who will need respiratory support with helmet continuous positive airway pressure.

Keywords Ultrasound · Bronchiolitis · Children · Pocus · Lung · Precision medicine

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Abbreviations

ANOVA	Analysis of variance
AAP	American Academy of Pediatrics
ED	Emergency department
HCPAP	Helmet continuous positive airway pressure
HFNC	High-flow nasal cannula
IQR	Interquartile range
LUS	Lung ultrasound
NICE	National Institute for Health and Care Excellence
PICU	Pediatric intensive care unit
POCUS	Point-of-care ultrasound
RSV	Respiratory syncytial virus
SaO ₂	Hemoglobin oxygen saturation
SD	Standard deviation
SPSS	Statistical Package for the Social Science

Introduction

Bronchiolitis is the main cause of lower respiratory tract infection in children younger than 24 months, as defined by the National Institute for Health and Care Excellence (NICE) [2] and American Academy of Pediatrics (AAP) [18] guidelines. It is the leading cause of hospitalization below the first year of life and usually manifests as an epidemic. The respiratory syncytial virus (RSV), in its subtypes A and B, is the main cause of bronchiolitis being isolated in 50 to 80% of the aspirated nasopharyngeal [11, 15, 16]. The main causes of hospitalization are hypoxemia (because it requires treatment with oxygen therapy, either invasive or not) and poor feeding ability (needing either intravenous fluids or nasogastric feeding) [17].

The diagnosis is clinical and essentially based on the anamnesis and the clinical evaluation. All guidelines do not recommend routine laboratory, diagnostic, or radiological examinations [2, 18]. In particular, it is difficult to distinguish a pneumonia from an atelectasis using a chest X-ray and this often leads to unnecessary antibiotic use because the risk of bacterial pneumonia is low. Conversely, a chest X-ray can be considered if the child has more of 2 days of fever, an asymmetric chest exam, an unusually high O₂ need, or a not demonstrated improvement [21].

In the last few decades, lung ultrasound (LUS) took place as support to clinical examination in course of neonatal and pediatric respiratory diseases as a valid tool for evaluating the lung parenchyma without subjecting the child to ionizing radiations [4–6, 19]. This examination is, in fact, inexpensive, non-invasive, rapid, and easily repeatable and can be carried out, after appropriate training, even by non-specialist radiologists (point-of-care ultrasound, POCUS). Furthermore, currently, the patient's bed ultrasound is considered a method of interest in the concept of "personalized medicine," allowing a more detailed evaluation of the individual patient in the

context of the single pathological condition and thus, a personalized care patient-based instead of disease-based [10].

In this perspective, it is essential for the pediatrician working in the emergency department (ED) to use these new tools in the attempt to identify patients requiring hospitalization for the continuation of treatment. In the field of bronchiolitis, Tomà et al. [24] have already demonstrated how diaphragm ultrasound can identify children requiring oxygen therapy, while the data about the utility of LUS in this setting are still few and not definitive. For this reason, in our study, we aimed to evaluate the existence of a correlation between clinical and LUS and the predictive value of LUS on requiring respiratory support in infants with bronchiolitis.

Materials and methods

Study design

We conducted a prospective study from January 1, 2017, to March 31, 2018.

The study was approved by the Ethics Committee of our Institution (number 1444_OPBG_2017), and fully informed consent from the parents of each participant was obtained before the study.

Children with a clinical diagnosis of bronchiolitis according to AAP guidelines ("a constellation of clinical symptoms and signs including a viral upper respiratory prodromes followed by increased respiratory effort and wheezing in children less than 2 years of age") were evaluated [18]. Only infants from 1 to 12 months of age were included, in order to reduce biases of selection. Infants with life-threatening disease requiring immediate intervention, preterm, with cardiac diseases, previous surgical conditions, comorbidities, genetic disorders, or disability were excluded.

Patients

All patients underwent a routine clinical evaluation in the emergency department by the pediatrician who defined the clinical severity according to the severity score of the Seattle Children's Hospital [21]. This score was created by the Seattle Children's Hospital in 2011 to assess infants with bronchiolitis and to define those who needed hospitalization (department of medicine or intensive care) from those who could be discharged.

The score is evaluated in three different age groups (<2 months, 2–12 months, 1–2 years):

- respiratory rate
- retractions: subcostal, intercostal, or supraclavicular retractions; nasal flaring; or bobbing of the head

- signs of dyspnea: reduction/suspension of feeding, reduction/suspension of vocalization, agitation, drowsiness, or confusion
- auscultation: inspiratory wheeze, expiratory wheeze, or reduction of air penetration

A grading of disease severity was obtained according to current scale (see ref [21]):

- (A) Mild bronchiolitis: score 1–4
- (B) Moderate bronchiolitis: score 5–8
- (C) Severe bronchiolitis: score 9–12
- (D) Healthy infant: score 0

Infants with mild bronchiolitis (score ≤ 4) at first evaluation with adequate feeding were discharged home after caregiver teaching (sign of respiratory distress, maintaining of adequate hydration, and technique of nasopharyngeal suction) and with follow-up established. Infants with moderate bronchiolitis (score 5–8) were hospitalized or discharged after evaluation of individual cases. Infants with severe bronchiolitis (score ≥ 9) at baseline or after breastfeeding were hospitalized.

Infants with hypoxemia (defined as oxygen saturation below 90% awake and 88% while sleeping) or with a degree of dehydration requiring intravenous fluid's administration were admitted, as well as those who reported or presented apneas.

Low family compliance was considered as a potential risk factor before discharging the patient and represented an additional criterion of hospitalization. Pediatric resuscitation was considered in the case of apnea associated with bradycardia and cyanosis, respiratory failure, and suspected intoxication.

Once admitted, nasopharyngeal aspirates were performed in all cases, as well as cardio-respiratory monitoring and anthropometric parameter (weight and length) evaluation.

The hospitalized infant, after clinical evaluation and monitoring of vital parameters, began oxygen therapy with low-flow nasal cannulas if the oxygen saturation was less than 90% in wakefulness or 88% in sleep.

In case of persistence of a $\text{SaO}_2 < 90\%$ despite therapy with low-flow oxygen or a clinical score persistently higher than 9 or a $\text{PaCO}_2 > 50$ mmHg or $\text{PaO}_2 \leq 60$ mmHg at the arterial hemogasanalyses, oxygen was administered with high-flow nasal cannula (HFNC).

Helmet continuous positive airway pressure (HCPAP) was used when there was no clinical improvement after 36 h of HFNC assessed in terms of heart rate, respiratory rate, clinical score, SaO_2 , PaCO_2 , and PaO_2 .

Mechanical ventilation was performed in all those infants in whom there was no clinical improvement after 36 h of HCPAP assessed in terms of heart rate, respiratory rate, clinical score, SaO_2 , PaCO_2 , and PaO_2 or acute respiratory failure.

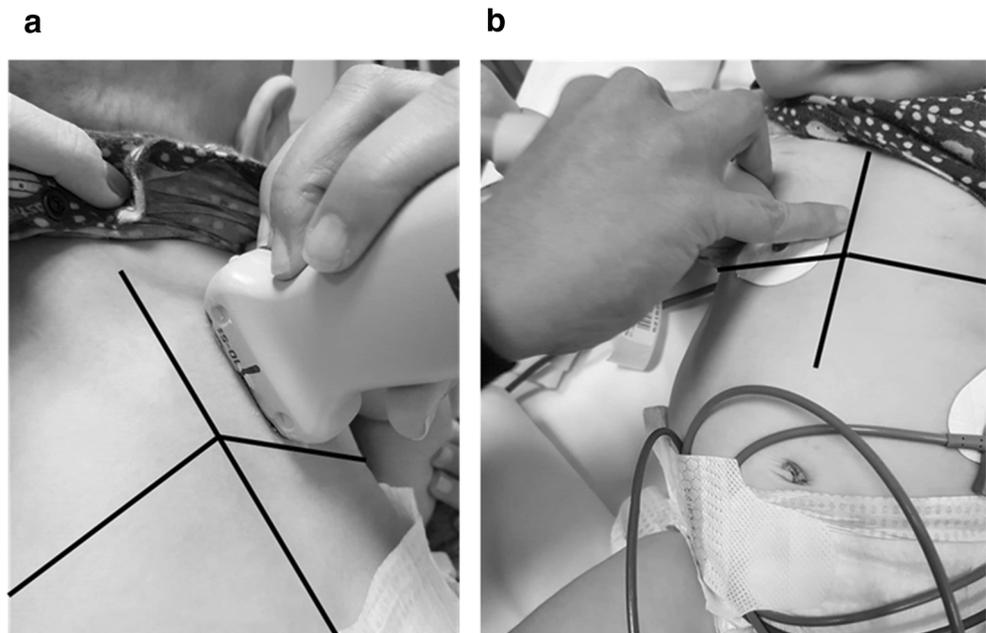
Lung ultrasound

Immediately after the first clinical examination in the emergency department (unless the patient was in critical conditions), chest ultrasound scans were acquired by two pediatricians with 5 years of experience in chest ultrasound.

We used a portable Doppler ultrasound machine (SonoSite M-Turbo) with a 10–12-MHz linear transducer.

Ultrasonography examinations were performed following the methodology previously described by Copetti et al. [4, 5]. Each hemithorax was divided into three areas: 1

Fig. 1 Patient positioning during ultrasound scans: **a** sitting position, **b** semi-recumbent position



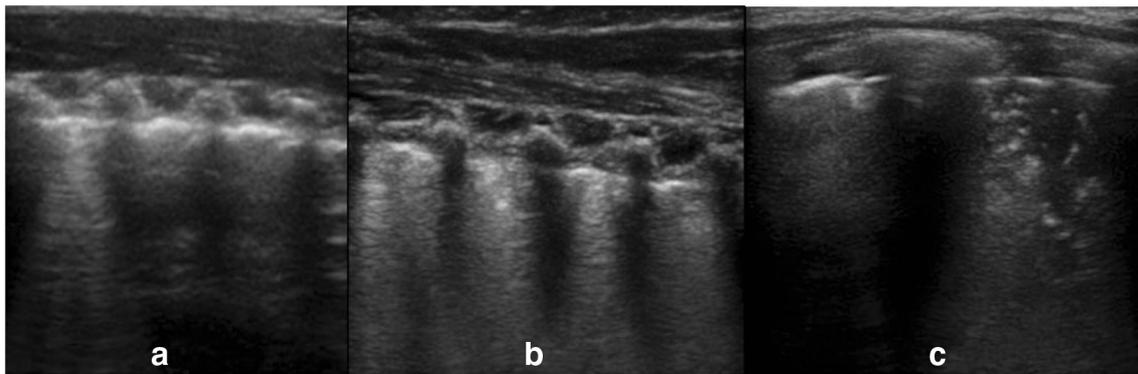


Fig. 3 Ultrasound score: **a** mild interstitial syndrome, **b** white lung, **c** subpleural consolidation > 1 cm

- 2: subpleural consolidation > 1 cm (Fig. 3c)

Therefore, the ultrasound score can vary between 0 and 24. Ultrasonographic recordings were stored on compact disks.

Outcome measures

- Primary outcome: to evaluate if the ultrasound score is able to predict who among infants with bronchiolitis will need respiratory support (non-invasive ventilation using HFNC/CPAP).
- Secondary outcome: to evaluate the existence of a correlation between clinical presentation and ultrasound score at the first evaluation in the emergency department.

Statistical analysis

Statistical analysis was performed using the SPSS software (IBM Statistical Package for the Social Science Statistics, version 24.0, Chicago, IL). The normality of the data distribution was assessed by the Kolmogorov-Smirnov test. Values were expressed as arithmetic means \pm standard deviation (SD) for continuous variables, median and interquartile range (IQR) for nonparametric data, or number and percentage (%) for categorical variable. The Mann-Whitney test, Student's *t* test, and one-way analysis of variance (ANOVA) were used to compare nonparametric and normal data respectively while the χ^2 was used to compare categorical variables. The Pearson (normal data) or Spearman (nonparametric data) tests were used for correlation analysis between variables. A multiple linear regression analysis (stepwise method) was performed with oxygen use time as the dependent variable and oxygen saturation at admission, echographic and clinical score, and echographic parameters as independent variables.

The rescued images were subsequently reviewed by the same operators who defined the score. Inter-observer reliability with Cohen's kappa was defined: 0.81 ± 1.00 excellent,

0.61 ± 0.80 good, 0.41 ± 0.60 moderate, 0.21 ± 0.40 fair, $> 0 \pm 0.20$ slight, and 0 absent. A *p* value < 0.05 was considered statistically significant.

Results

We evaluated 76 previously healthy infants (median age 90 days [IQR 62–183 days], 53.9% males).

The symptoms were onset 2 (1.2–3.8) days before to ED evaluation. In nasopharyngeal aspirates, the respiratory syncytial virus was isolated in 33 (43.4%) patients, in particular

Table 1 General and clinical characteristics for the study population

Patient number 76	
Age, days (IQR)	90 (62–183)
Sex, males no. (%)	41 (53.9)
Weight, kg (SD)	6.07 (± 1.66)
Height, cm (SD)	60.89 (± 7.07)
Heart rate, bpm (SD)	145.30 (± 28.38)
Respiratory rate, breath/min (SD)	48.0 (± 12.12)
Mean SaO ₂ in ED, % (SD)	97.55 (± 3.42)
RSV, no. (%)	33 (43.4)
RSV B, no. (%)	17 (51.5)
Coinfection, no. (%)	16 (21.0)
Time from onset to ED evaluation, days (SD)	2 (1.2–3.8)
Respiratory support, no. (%)	41 (53.9)
Oxygen therapy, h (IQR)	120 (48–168)
Low-flow oxygen with nasal cannula, no. (%)	9 (22)
HFNC, no. (%)	32 (78)
HCPAP, no. (%)	13 (31.7)
Mechanical ventilation, no. (%)	3 (7.3)

Variables are expressed as frequencies (percentages), arithmetic means (\pm SD), or median (interquartile range, IQR). ED, emergency department; SaO₂, hemoglobin oxygen saturation; RSV, respiratory syncytial virus; HFNC, high-flow nasal cannula; HCPAP, helmet continuous positive airway pressure

Table 2 General and clinical characteristics for the study population according to respiratory support

	No respiratory support (no. 35)	Respiratory support (no. 41)	<i>p</i>
Males, no. (%)	19 (54.3)	22 (53.7)	ns
Age, days (IQR)	127.00 (73–195)	83 (54–182)	ns
Age ≤ 3 months, no. (%)	25 (71.4)	31 (75.6)	ns
Weight, kg (SD)	6.76 (± 1.45)	5.74 (± 1.67)	0.03
Height, cm (SD)	62.60 (± 5.21)	60.15 (± 7.67)	ns
Heart rate, bpm (SD)	141.05 (± 23.08)	148.32 (± 31.63)	ns
Respiratory rate, breath/min (SD)	45.22 (± 13.22)	49.78 (± 11.19)	ns
Time from onset to ED evaluation, days (SD)	2.5 (1–4.5)	2 (1.75–3)	ns
Days of admission, days (SD)	1 (0–4)	4.5 (7–10)	0.001
Mean SaO ₂ in ED, % (SD)	99.00 (± 1.58)	96.39 (± 4.03)	0.002
RSV +, no. (%)	7 (20)	26 (63.4)	ns
Coinfection, no. (%)	5 (14.3)	9 (22)	ns
Clinical score			0.001
Mild, no. (%)	25 (71.4)	6 (14.6)	
Moderate, no. (%)	10 (28.6)	28 (68.3)	
Severe, no. (%)	0 (0)	7 (17.1)	
Ecographic score	1 (0–3)	2 (1–4)	0.006

Variables are expressed as frequencies (percentages), arithmetic means (± SD) or median (interquartile range, IQR). ED, emergency department; SaO₂, hemoglobin oxygen saturation; RSV, respiratory syncytial virus; ns, not significant

the subtype B was in 17 (51.5%), while two or more virus were present in 16 (21.0%). General and clinical characteristics of sample are described in Table 1.

21.1% children were discharged and 78.9% were admitted for a median length of 5 days (IQR 4–8); 2 of 60 children (3.3%) were directly admitted to the pediatric intensive care unit (PICU).

Forty-one infants required oxygen therapy of which 9 (22%) via nasal cannula with low-flow oxygen and 32 (78%) with HFNC. Thirteen infants (31.7%) who initially needed HFNC then shifted to HCPAP, while for 3 infants (7.3%), mechanical ventilation was needed. Table 2 shows

the main characteristics for the study population according to respiratory support.

Considering the clinical score, children with higher score had a higher probability of requiring respiratory support (*p* 0.001; Table 2, Fig. 4); moreover, a statistically significant difference was found in the oxygen saturation upon arrival in ED (*p* 0.001) and in the duration of oxygen therapy during admission (*p* 0.002) confirmed with the post hoc test (Bonferroni) (Table 3, Fig. 5).

At the ultrasound evaluation, there was a significant difference on ultrasound score between those who needed

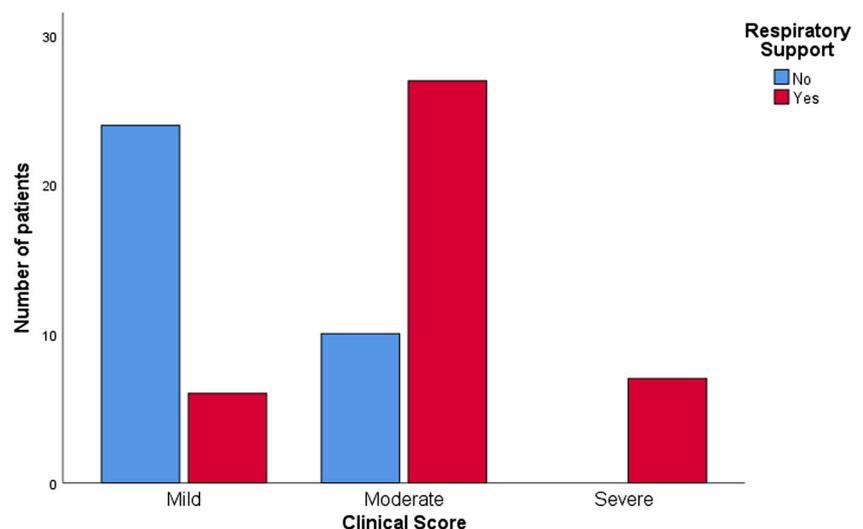
Fig. 4 Difference in clinical score based on the need for respiratory support

Table 3 Difference in SaO₂ and duration of oxygen therapy during admission according to clinical score

	Clinical score			<i>p</i>	Bonferroni post hoc test (<i>p</i>)		
	Mild	Moderate	Severe		1 vs 2	1 vs 3	2 vs 3
Mean SaO ₂ in ED, % (SD)	99.5 (± 0.88)	97.29 (± 3.01)	91.33 (± 4.41)	0.002	0.007	0.001	0.001
Oxygenotherapy, h (SD)	0 (0–0)	48 (0–144)	132 (90–168)	0.001	0.005	0.025	ns

Variables are expressed as arithmetic means (± SD) or median (interquartile range, IQR). ED, emergency department; SaO₂, hemoglobin oxygen saturation; ns, not significant

respiratory support or not (*p* 0.003, Fig. 6). With the Spearman coefficient, no correlation was found between the score obtained on the pulmonary ultrasound and the saturation of oxygen upon arrival in ED, while it was evident with the duration of oxygen therapy during admission (*p* 0.003, *r* 0.35). Infants who needed ventilation with HCPAP had a more severe ultrasound score (2 (3–4) vs 1 (1–3), *p* 0.028) (Fig. 7) and clinical score (7 (5–9) vs 5 (2.5–6), *p* 0.004) than those who did not need it. Linear regression using a stepwise method using oxygen hours as a dependent variable and oxygen saturation at the entrance, age, clinical score, and ultrasound score of bronchiolitis as independent variables showed a model that includes the clinical score as the only explanatory variable (*r* 0.42, *R*² 0.17, *p* 0.001, *t* 3.54) (Table 4).

The inter-rater agreement was 0.925 (95% CI, 0.855–0.957) with Cohen’s kappa coefficient of 0.81.

Discussion

In this study, we showed that both clinical and ultrasound scores were able to predict the need for oxygen support in infants with bronchiolitis evaluated in the ED. Moreover, the ultrasound score was found to correlate with the need of respiratory support (HFNC or HCPAP).

To our knowledge, this is the first study evaluating the severity of bronchiolitis from a clinical and ultrasound

point of view in previously healthy infants during the first assessment carried out directly by the emergency pediatrician in the ED.

Bronchiolitis is the first cause of hospitalization below the first year of life [2] determining an important economic expenditure in Western countries [8]. The main reason for hospitalization is hypoxemia that requires adequate ventilatory support since currently there are no effective pharmacological therapies able to reduce the disease duration. It is therefore essential for the pediatrician working in the ED to look for new tools to identify those patients who need hospitalization for the continuation of treatment.

In fact, the concept of prevention and treatment strategies that take individual variability into account (the so-called precision medicine) is emerging as a priority [3]. Traditionally, genomic and proteomic concepts have been included in this individualized approach [12]; however, the concept of precision medicine can be easily applied to POCUS as suggested by a recent review by Kessler et al. [10]. In this scenario arises the need to perform pulmonary ultrasound in the infant affected by bronchiolitis already in the ED, in order to add new data at clinical evaluation [20].

We chose the ultrasound score proposed by Taveira et al. in 2018 as, in our opinion, it is easy to perform and consents a detailed overlook of all pulmonary fields. In our population, we obtained an average score of 2 [2, 11, 18] with a maximum

Fig. 5 Difference in duration of oxygen therapy during admission based on the clinical score

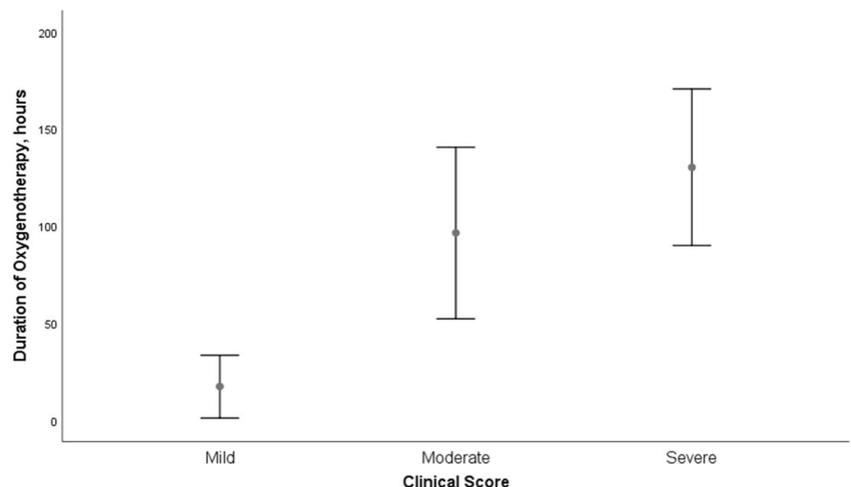
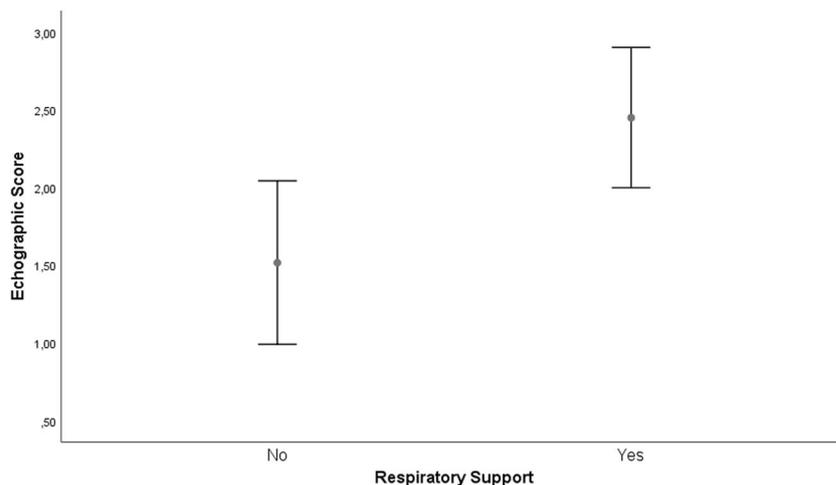


Fig. 6 Difference in ecographic score based on the need for respiratory support



score of 24 [23]. Our average score was similar to the one obtained by Taveira et al.

The ultrasound score in our study did not correlate with oxygen saturation on arrival in the ED but with the duration of oxygen therapy during hospitalization (p 0.003, r 0.35). This data complies with what previously highlighted by Taveira et al. [23]. In addition, the scores obtained were higher in infants who needed respiratory support with HCPAP (mean score 2 (3–4) vs 1 (1–3), p 0.028). This is an important finding, since an early individuation of stable patients whose clinical conditions can rapidly deteriorate is essential for the management of the patient in the ED.

In accordance with previous studies [13, 14], our infants affected by severe forms of bronchiolitis, initially requiring HFNC, often needed to be switched to HCPAP and then to be transferred in PICU.

Importantly, despite the clinical score had a direct correlation with the duration of oxygen therapy during hospitalization (p 0.0001, r 0.53), it presented an inverse correlation with

oxygen saturation upon arrival in ED (p 0.0001), r - 0.55) and was not predictive of HFNC either HCPAP support, contrary to LUS.

Disease severity is significantly worse in children with RSV [7]. As a matter of fact, in our study, 63.4% of children RSV positive needed respiratory support.

Recently, we also demonstrated the role of diaphragm ultrasound on a case series of children with bronchiolitis, describing a number of diaphragm parameters able to predict bronchiolitis severity [1].

In the current study, we did not evaluate diaphragm function, but we can affirm that both lung and diaphragm evaluation, along with clinical findings, can be helpful for the physician and should be included in the routine evaluation of infants with bronchiolitis.

Our study has a number of limitations. First, like all ultrasound examinations, it is an operator-dependent technique and is associated with a learning curve. To minimize variability, even though the ultrasounds were performed by only two emergency pediatricians with pulmonary ultrasound training,

Fig. 7 Difference in ecographic score based on the need for respiratory support with HCPAP

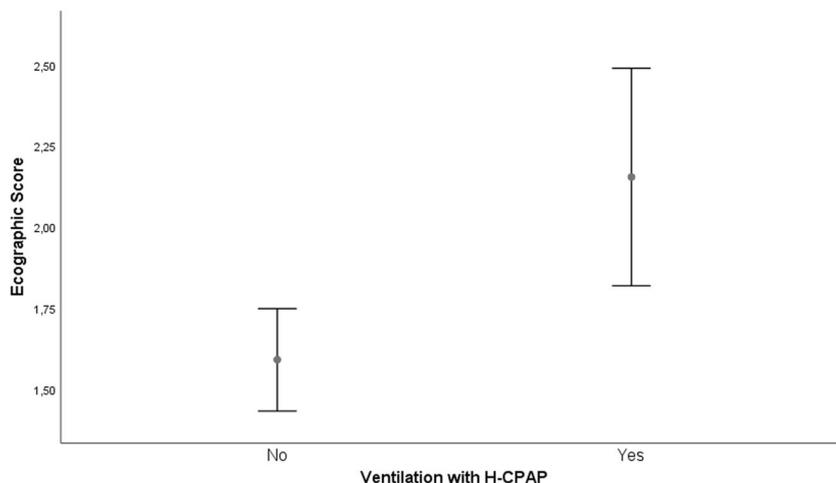


Table 4 Multiple linear regression analysis for hours of oxygen delivery as dependent variable

	β -coefficient	<i>t</i>	<i>p</i>
Clinical score	0.389	3.268	0.002
Age	0.051	0.423	0.055
Mean SaO ₂ in ED	−0.68	−0.445	0.658
Ecographic score	0.146	1.224	0.226
	$R = 0.389$	$R^2 = 0.151$	

ED, emergency department; SaO₂, hemoglobin oxygen saturation

the rescued images were subsequently reviewed by the same operators who defined the score. Our calculated Cohen's kappa was 0.81, which means that the inter-observer agreement between the pediatric operator's interpretation was excellent. The evidence of an excellent inter-observer agreement between two operators suggests that lung ultrasound is not only easy to perform but also easy to read.

Secondly, since there is no agreement in the literature on age interval to define a bronchiolitis, we enrolled only infants with age between 1 and 12 months [9, 22, 25].

Thirdly, in our study, we had only seven infants diagnosed with severe bronchiolitis and then few patients had high scores (median of 2 points) in an ultrasound-based scale with a maximum possible score of 24 points.

We hypothesize that by increasing the number of patients, especially those affected by severe forms and requiring mechanical ventilation, it will be possible to point out a greater difference in the ultrasound scores and therefore to more easily identify those who need an early transfer in PICU.

In conclusion, our study shows that LUS in infants affected by bronchiolitis may be a useful, rapid, and non-invasive method to be integrated with the clinical evaluation in order to better define the prognosis of the individual patient, even at the first assessment in the ED. Multicenter studies on larger populations are necessary to confirm these data. In the era of precision medicine and the spread of POCUS, if our data would be confirmed, we believe that the scores obtained by lung and diaphragm ultrasound could be combined into the clinical scores by creating a new single comprehensive score to be routinely used during every evaluation of a child with bronchiolitis.

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Authors' contribution Conception and research design: M.C. Supino, D. Buonsenso, A.M. Musolino

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Data analysis and interpretation and drafting the article: A. Reale, B. Scialanga, E. Gigliani, M.C. Supino

Final approval of the article: all the authors.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study described has been carried out in accordance with the abovementioned standards and has been approved by the institutional ethic committee.

Informed consent Informed consent was obtained from all individual participants included in the study.

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