

Ultrasound detection of pneumonia in febrile children with respiratory distress: a prospective study

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Received: 29 December 2014 / Revised: 20 July 2015 / Accepted: 30 July 2015 / Published online: 19 August 2015
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Abstract To analyse the usefulness of bedside lung ultrasound (LUS) in detecting lung consolidation in a paediatric emergency room (ER) setting, febrile children seen at our ER from 2008 to 2012 with a moderate to severe respiratory distress underwent LUS, chest X-ray (CXR) and laboratory investigations. At first ER assessment, LUS identified a lung consolidation in 207 patients of 222 children enrolled, with a *liver-like appearance* in 75 (36.2 %) and an associated pleural effusion in 36.7 % of cases. CXR proved positive in 197 cases, showing a *parenchymal*

consolidation (68.5 %) or a *focal ground-glass opacity* (31.4 %). LUS liver-like consolidation was significantly associated with longer duration of fever ($p=0.002$), higher neutrophil counts and C-reactive protein (CRP) values ($p=0.015$ and $p<0.0001$, respectively), and with the discovery of a homogeneous and dense *parenchymal consolidation* on CXR ($p<0.0001$).

Conclusion: LUS can be adopted by the clinician as a non-invasive bedside tool to expand the physical evaluation of febrile children with respiratory distress. In our study, LUS results appeared not only as reliable as CXR

Communicated by Jaan Toelen

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Electronic supplementary material The online version of this article (doi:10.1007/s00431-015-2611-8) contains supplementary material, which is available to authorized users.

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in detecting lung consolidations but also consistent with clinical and laboratory data.

What is known:

- *The diagnosis of pneumonia is mainly based on physical examination plus radiologic and laboratory evaluation when needed.*
- *Although lung ultrasound (LUS) has shown high sensitivity in detecting several pleuropulmonary diseases in adults, its role in the work-up of pneumonia in children is not yet widely recognized.*

What is new:

- *LUS is confirmed to be a reliable imaging technique for the diagnostic work-up of febrile children with respiratory distress, consistent not only with CXR results as previously reported by others but also with clinical and laboratory data.*
 - *In the hands of trained clinicians, it may represent a valuable supplemental bedside tool for a rapid evaluation in such circumstances.*
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Keywords Lung consolidation · Chest X-ray · Lung ultrasound · Paediatrician

Abbreviations

CAP	community-acquired pneumonia
CRP	C-reactive protein
CXR	chest X-ray
ER	emergency room
LUS	lung ultrasound
PPE	parapneumonic pleural effusion
WBC	white blood cell

Introduction

The diagnosis of community-acquired pneumonia (CAP) is mainly based on patients' medical history and physical examination. However, in moderate to severe cases when imaging evaluation is needed, current guidelines indicate posteroanterior (PA) chest X-ray (CXR) as the investigation of choice in children [2, 5, 16]. Its major disadvantages include ionizing radiation exposure [3, 4], high inter-observer interpretation variability [11, 18, 30, 36], low sensitivity compared to CT scan [17, 37], difficulty in exploring up to 40 % of lung area through a single projection (due to overlying cardiac, mediastinal and sub-diaphragmatic structures) [7] and practical delays for obtaining and processing images.

Published data in adults [10, 14, 23, 26, 28, 31, 32, 39], and to a lesser extent in children [6, 9, 19, 20, 33, 35, 39], point to the usefulness of lung ultrasound (LUS) as an alternative to traditional CXR imaging in detecting lung consolidations, including those due to pneumonia. Previous studies utilizing CT scan as the reference standard showed that LUS imaging outperformed CXR in diagnosing pneumonia in adults [10,

26, 28, 32], with remarkable sensitivity and specificity (up to 90 and 97 %, respectively) [32].

Once a lung pathologic process, causing air replacement by fluid, reaches the pleural surface, it can be visualized by ultrasound as a consolidation [1, 23]. Literature on adults suggests that lung consolidations extend to the pleura in about 92 % of cases in in-patients [32] and up to 98 % of cases in critically ill patients [23]. Previous evidence [6, 9, 19, 20, 35] and the anatomical characteristics of the child's thinner chest wall and smaller lung volume suggest the possibility of even better results in the field of paediatrics.

In this study, we investigated the usefulness of bedside LUS and CXR in detecting lung consolidations in a paediatric emergency room (ER) setting. Moreover, to reinforce the diagnosis of pneumonia, we analysed the relationship between sonographic findings at presentation and clinical and laboratory data.

Patients and methods

From February 2008 to February 2012, a total of 222 febrile children seen at the ER of our Paediatric Department with moderate to severe respiratory distress [2, 5, 16] were enrolled in this prospective study. The study was approved by the ethics committee of our institution. Parents of all eligible cases accepted to participate in the study and gave informed written consent. To avoid an excess of radiological investigations, we focused our study on a highly selective population, using the following inclusion criteria:

- Age (3 months–16 years)
- Triage temperature >38.5 °C
- Moderate to severe respiratory distress (defined as ≥ 1 of the following criteria: respiratory rate >70 breaths/min within 1 year of age or >50 breaths/min in older children, moderate to severe breathlessness, moderate to severe retractions, nasal flaring, grunting respiration, oxygen saturation <92 % on room air)

Children with respiratory distress clearly due to asthma or with a clinical diagnosis of mild to moderate bronchiolitis were excluded. At first evaluation, enrolled patients underwent LUS and subsequently CXR and blood tests. Such investigations were always performed in this sequence. All LUS scans were done in our ward by one of the three paediatricians with specific LUS expertise, blinded to detailed clinical data. All three had attended a specific course on LUS and supervised practical training. The presence of one of the three (available for about 80 h weekly) was, therefore, necessary for patient enrolment. A high-resolution 7.5–10-MHz linear probe was used, occasionally supplemented by a 3.5–5-MHz convex probe (MyLAB 25, Esaote Medical Systems, Italy).

LUS was performed following a pre-defined scanning scheme according to current literature [9, 23, 39]; the probe was placed perpendicular and parallel to the ribs in the anterior and lateral (lying patient) and posterior (sitting patient) lower and upper thorax, along the conventional hemiclavicular, parasternal and axillary lines. Pleural effusion was systematically searched for at the level of the anterior, lateral and posterior costophrenic angles and in the areas adjacent to lung consolidation. Posteroanterior CXR in supine or standing position was analysed by the radiologist on duty, informed about clinical conditions but unaware of LUS findings. At the radiologist's discretion, additional projections were obtained in selected cases.

The criterion to define a positive LUS was the finding of a lung consolidation with evidence of sonographic air bronchograms [39]. LUS results were classified into specific pattern categories based on the literature [9, 23, 25, 31, 33] (Table 1). CXR was assessed for the presence of patterns such as *parenchymal consolidation*, *focal ground-glass opacity* or *alveolar-interstitial syndrome* [15].

In all cases with radiographic demonstration of lung consolidation but sonographically negative, a second LUS was performed shortly after by a second operator informed about CXR findings to further assess the actual reliability of the technique. On the other hand, in case of negative CXR and positive LUS, radiograms were subsequently reviewed by chest radiology experts, blinded to LUS findings.

When a diagnosis of lung consolidation was achieved, the response to antibiotic therapy (defervescence and amelioration of general and respiratory conditions) was assessed within 24–48 h and the complete disappearance of LUS findings 1 month later.

Statistical analysis

Sample size calculations to assess the agreement between LUS and CXR were based on McNemar's test [27]. Assuming a proportion of discrepancies between the findings obtained

Table 1 Lung ultrasound patterns

Normal pattern	Normal lung sliding, regularly echogenic pleural line with a predominant A-line artefact pattern
Lung consolidation	Hypoechoic area with irregular margins and adjacent comet-tail artefacts along a non-homogeneous echo texture. Hyperechoic images represent air bronchograms arborizing within the lesion
	Liver-like ("hepatized") area with fluid and air bronchograms (static or dynamic)
Alveolar-interstitial syndrome	Multiple B-line artefacts arising from the pleural line and spreading up to the edge of the screen erase the A-lines and move consensually with lung sliding

with the two techniques comparable to that reported by Copetti and Catarossi [9], with $\alpha=0.05$ and $\beta=0.01$, a minimum of 195 children were estimated to be enrolled.

Differences in the distribution of categorical variables between groups of subjects were analysed through the chi-square test or Fisher's exact test. Differences in the distribution of continuous variables among groups of subjects were analysed through the Kruskal-Wallis test or the Wilcoxon test. The agreement between LUS and CXR results was assessed through McNemar's test. Since CXR cannot be considered as a gold standard for the diagnosis of pneumonia [17, 37], we did not calculate any accuracy measures such as sensitivity or specificity. Instead, we calculated the overall percent agreement (OPA) and the positive and negative agreement (PA and NA) between LUS and CXR [8]. All statistical analyses were performed using SAS Enterprise Guide v4.3 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 222 patients [mean age 4.9 ± 3.1 (range 0.16–16); 114 females] were enrolled in the study (Table 2). Seventy-five of them (33.8 %) were admitted for intravenous antibiotic therapy and/or rehydration. Radiographic and LUS investigations were successfully performed in all; in 121 (54.5 %) cases, a double-view (PA plus lateral) CXR was performed based on the radiologist's judgment. Four patients with empyema also underwent chest CT scan which confirmed both CXR and LUS findings.

Table 2 Clinical characteristics

	Number of patients	Percentage of patients
Temperature at triage (°C)		
38.5–39.5	210	94.6
>39.5	12	5.4
Age-specific tachypnoea at triage	180	81
Oxygen saturation at triage (%)	197	88.7
97–100	62	31.5
93–96	95	48.2
<92	40	20.3
Duration of fever (h)		
<24	28	12.6
24–48	49	22.1
>48	145	65.3
Cough	199	89.6
Chest pain	103	46.4

Distribution of specific clinical features among the total patient cohort (222 children)

LUS and CXR findings

At first ER assessment, 190 children showed evidence of lung consolidation both on CXR and LUS. In another 17 cases, all showing echographic consolidation, CXR gave negative results, while 7 CXR-positive cases were not detected by LUS on first instance but were confirmed by the second operator. Eight cases proved negative with both techniques (Table 3).

The CXR review confirmed negativity in 10/17 cases, whereas in 7 a *focal ground-glass opacity* image was described, mainly localized at the left pulmonary base (6/7). In 5 of these cases, 2 projections were available. All 17 CXR-negative and LUS-positive consolidations were located at the posterior costophrenic angles, 13 on the left (76 %) and 4 on the right side.

In Table 4, LUS and CXR findings (including second assessment) are shown. Of the 214 consolidations eventually detected by LUS, in most cases (139/214), lung consolidation was recognized by LUS as a subpleural hypoechoic area with irregular margins and underlying B-line artefacts (Fig. 1). In the remaining 75 cases (35 %), LUS showed a marked *liver-like appearance* of the consolidated lung (Video 1) with an irregular lower boundary and with arborized hyperechoic areas within. In 39 cases, both morphologic patterns coexisted. Lung sliding (Video 2) was described as reduced but present in all cases, and in no case a “lung pulse” sign was recognized [24].

With regard to the side of consolidation, 16 cases were bilateral (all confirmed by both techniques), 106 involved the right lung, 92 the left lung (14 % of the latter missed by CXR at first assessment vs. 3 % missed by LUS; $p=0.05$).

A *liver-like appearance* of the consolidated lung on LUS was significantly associated with evidence of a homogeneous and dense opacification—*focal parenchymal consolidation*—on the subsequent CXR [64/75 (85 %) cases; $p<0.0001$].

Parapneumonic pleural effusion (PPE) at presentation was identified by LUS in 76/214 (35.5 %) cases. Only 40 effusions were detected by CXR, 8 of which not confirmed by LUS. Surgical drainage was applied in 17 cases, corresponding to 7.9 % of CAP cases.

Table 3 Sonographic and radiographic findings at first assessment, before review of discordant cases

	CXR-	CXR+	Total
LUS-	8	7	15
LUS+	17	190	207
Total	25	197	222

LUS lung ultrasound, CXR chest X-ray
 p value of McNemar's test 0.0412; POA = 0.89 (95% CI 0.85–0.93); PA = 0.94 (95% CI 0.92–0.96); NA = 0.40 (95% CI 0.21–0.59)

Table 4 Morphology of sonographic and radiographic findings

LUS	
Lung consolidation with air bronchograms	214
- Hypoechoic area with heterogeneous echo texture ($n=139$)	
- Hepatization ($n=75$)	
Alveolar-interstitial syndrome	10
Pleural effusion	76
CXR	
Focal ground-glass opacity	69
Focal parenchymal consolidation	135
Alveolar-interstitial syndrome	6
Pleural effusion	40

Distribution of specific echographic and radiographic patterns including second assessment of discordant cases. Alveolar-interstitial syndrome coexisted with lung consolidation

LUS lung ultrasound, CXR chest X-ray

Clinical features

Defervescence was achieved within 48 h from new antibiotic treatment onset in 192/214 (89.7 %) cases. In 47/214 (21 %), who were already on antibiotic treatment (macrolide or low-dose amoxicillin) when first seen at our ER, dosage or drug had to be changed. No significant association was found between previous antibiotic treatment and the hepatization process ($p=0.39$).

There was a statistically significant association between lack of defervescence at 48 h and the presence of pleural effusion on first LUS assessment. In fact, of the 30 patients in whom fever did not respond within 48 h, 6 were negative on both imaging techniques and 24 (80 %) displayed a PPE. Conversely, a pleural effusion was detected in only 27 % (52/192) of those with prompt fever resolution ($p<0.0001$).

Regarding imaging categories, when *liver-like consolidation* pattern was detected by LUS, fever at



Fig. 1 Lung consolidation with sonographic air bronchograms, as a subpleural hypoechoic area with irregular margins and underlying comet-tail artefacts

presentation had lasted for over 48 h in 58 (77 %) cases and for less than 24 h in only 4 cases ($p=0.002$). On the other hand, in 76 % (19/25) of patients with fever of less than 24-h duration, LUS showed a not hepatized pattern ($p=0.03$). Similarly, when considering CXR, fever of more than 48-h duration was present in 95/135 (70 %) cases with *parenchymal consolidation* and in only 58 % of those showing *focal ground-glass opacity* ($p=0.064$).

Notably, in 22/214 (10.2 %) patients with radiologically and sonographically confirmed lung consolidation, no abnormal auscultatory findings were present at first ER assessment, while in another 38 (18 %) cases, auscultatory evidence was equivocal. These groups' clinical features were similar to the other patients regarding duration of fever, respiratory signs and symptoms, percentage of previous antibiotic administration and treatment response. The same was true for the 17 patients with positive LUS and negative CXR at presentation.

Laboratory results

Laboratory data are reported in Table 5. Significantly higher neutrophil counts (median $14.916 \times 10^9/L$; $p=0.015$) and CRP values (median 256 mg/L; $p<0.0001$) were detected in patients with a LUS *liver-like consolidation* pattern, compared to the not hepatized pattern group (median neutrophil count $12.548 \times 10^9/L$ and median CRP 99 mg/L). A similar trend was found comparing CXR images with laboratory results; patients with *parenchymal consolidation* had significantly higher neutrophil and CRP values than the ground-glass group [median neutrophil count $14.670 \times 10^9/L$ vs. $12.574 \times 10^9/L$ ($p=0.06$) and median CRP 186 mg/L vs. 67 mg/L ($p<0.0001$)].

There was no statistically significant difference concerning WBC, neutrophil count and degree of inflammation between LUS and CXR concordant and discordant groups. Also, no difference was found in patients with negative (22) or equivocal (38) auscultatory evidence when compared to the general study population. On the contrary, the 8 cases with both CXR and LUS negative results showed lower WBC (median $6.273 \times 10^9/L$), neutrophils (median $3.335 \times 10^9/L$) and CRP (median 21 mg/L) (Fig. 2).

Discussion

The diagnosis of CAP, especially in paediatric age, is historically based on physical examination, while blood tests and microbiological and radiological investigations should not be performed routinely [2, 5, 16]. When an imaging assessment is clinically required, the recently revised British Thoracic Society guidelines recommend a PA chest X-ray film, considering the addition of the lateral view unhelpful [16]. The use of CT scan, the gold standard technique, is limited by its cost and the significant radiation burden [4, 5]. Although a recent international consensus conference [39] stated the reliability of lung ultrasound in evaluating pneumonia in adults and children, LUS is not currently included in the diagnostic work-up of paediatric CAP.

At ultrasound examination, lung consolidation due to pneumonia is detected either as a hypoechoic area with non-homogeneous echo texture, irregular margins and underlying comet-tail artefacts [9, 31] or as a liver-like appearing parenchymal area [23, 26, 33]. Arborized echogenic structures, representing air bronchograms, are also often seen within such images. Air can be seen moving through bronchi (dynamic air bronchogram), and this finding indicates pneumonia with a positive predictive value of 97 % [26], ruling out atelectasis [9].

In our series, LUS proved to be at least as reliable as CXR in detecting and locating a lung consolidation, confirming previous reports [9, 22, 23, 28, 32]. Our study did not allow us to determine LUS diagnostic accuracy, as the gold standard is undoubtedly CT scan, which cannot be routinely used in children for obvious ethical reasons. On the other hand, our findings showed LUS reliability to be at least comparable to that of CXR in diagnosing consolidations in febrile children with a clinically relevant respiratory involvement [2, 5, 16]. Notably, in our study population, mild uncomplicated cases, where CXR is not routinely performed, were not enrolled. This could represent a selection bias not allowing us to extend our results to mild cases. It is reasonable that similar LUS and CXR agreement could also be obtained in such circumstances, but at the same time, it is possible that small and localized parenchymal lesions do not reach the pleura, remaining undetectable by ultrasounds. These hypotheses need to be validated by further studies.

Table 5 Laboratory results

	LUS consolidations ($n=214$)	CXR-/LUS+ ($n=17$)	CXR-/LUS- ($n=8$)	p value of Kruskal-Wallis test
White blood cell count median	17.505	16.580	6.273	0.0043
Neutrophil count median	13.445	13.761	3.335	0.0035
C-reactive protein median, mg/L	128	112	21	0.0585

White blood cell and neutrophil counts are expressed as number of cells $\times 10^9/L$

LUS lung ultrasound, CXR chest X-ray

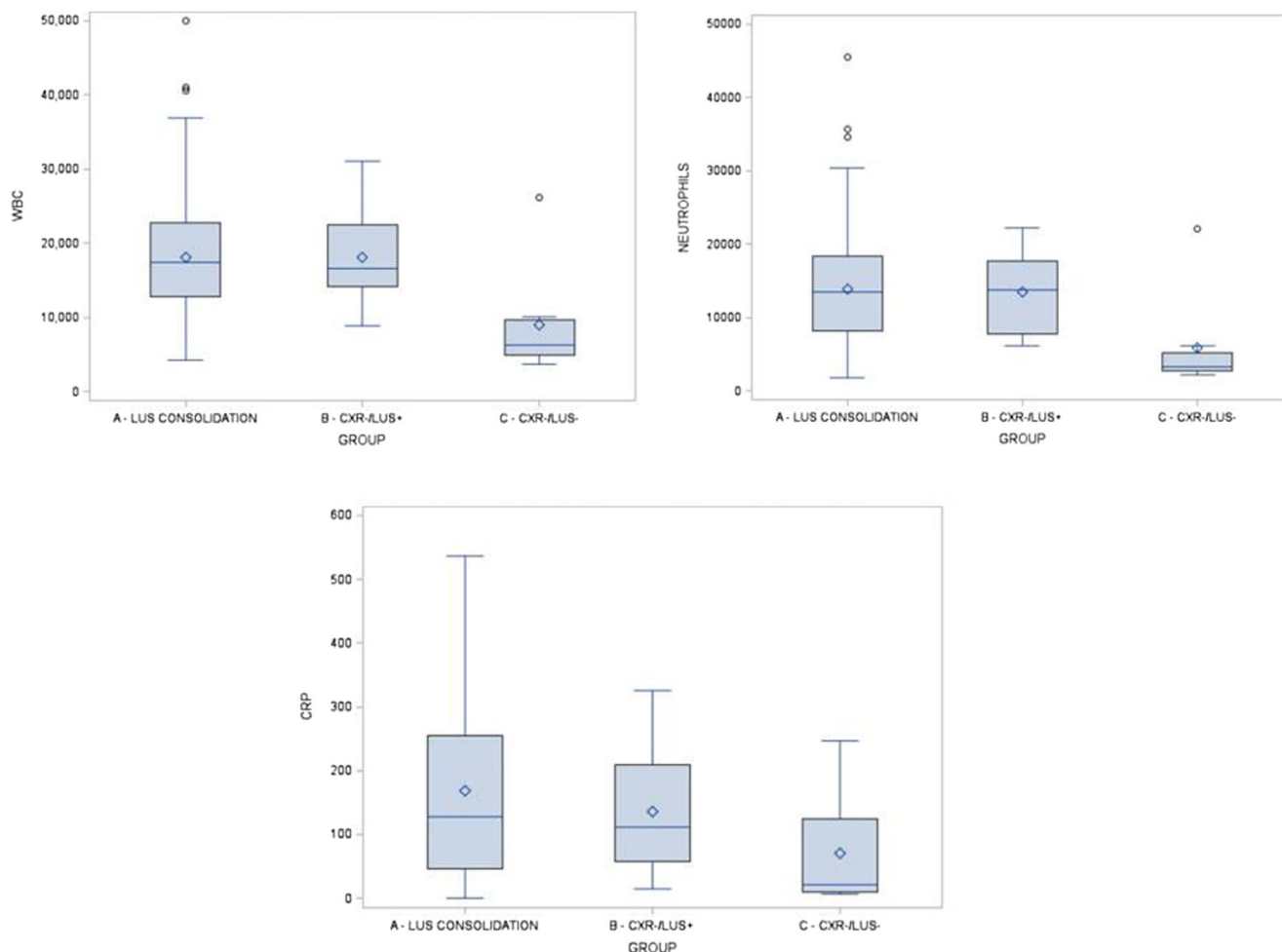


Fig. 2 Distribution of white blood cells, neutrophils and CRP by groups: LUS+, LUS+/CXR- and LUS-/CXR-

Considering LUS pathognomonic features of pneumonia [9, 23, 26, 31, 33], a definite diagnosis of CAP was achieved in all patients presenting a lung consolidation at first ER assessment. Pneumonia was sonographically recognized as a subpleural non-homogeneous hypoechoic area and/or a marked liver-like area, both with irregular margins and arborized air bronchograms within. Both morphologic patterns seem to be part of the same infectious process, but at different evolutive stages; along with the gradual decrease of air alveolar content due to inflammatory fluid filling, the hepatization process becomes increasingly appreciable. The longer duration of fever in most of our cases showing hepatized consolidation seems to be consistent with such an interpretation. Moreover, we found a significant association of higher neutrophil counts and CRP values with LUS evidence of more marked loss of aeration.

Although an unequivocal method to distinguish between bacterial and viral aetiology in CAP is lacking, literature data point to clinical features, prompt response to antibiotic treatment, leukocytosis ($>15 \times 10^9/L$), CRP ($>60 \text{ mg/L}$) and PCT values ($>0.5 \mu\text{g/L}$) as the best indicators of bacterial aetiology

[13, 34, 38]. The consistency of such data in the majority of our cases of lung consolidation, including those in which only LUS was positive, tends to reinforce the diagnosis of pneumonia and the likelihood of bacterial aetiology. Moreover, the few patients with completely negative imaging definitely had lower levels of such biomarkers (Fig. 2).

The lack of CT scan confirmation is a significant limitation to our study, especially in discordant cases (CXR negative-LUS positive), in which, however, the diagnosis of pneumonia was corroborated by the laboratory and clinical data (including prompt response to treatment). The clinical and laboratory characteristics of this small group of patients (17) were, in fact, comparable with all the unequivocally positive cases, excluding the hypothesis of an only initial, less marked or previously partially treated pneumonic process. Subdiaphragmatic and retrocardial localizations, known to be poorly imaged by a single frontal view [7], may account for CXR negativity, as was the case in all our 17 cases.

Of note, 28 % of patients revealed inconclusive auscultatory signs but received an immediate LUS diagnosis of lung consolidation, requiring only a few minutes, as previously

described [9, 10, 28]. Considering this proportion of equivocal cases at clinical ER evaluation, the refinement of the physical examination with such a bedside tool may allow for a wider rapid detection of lung consolidations (possibly documenting its location and associated complications) and thus immediate therapeutic decisions in an appreciable number of cases.

Ultrasonography is recognized to be as adequate as CT scan to identify even small amounts of pleural effusion, with sensitivity and specificity values approaching 100 % [12, 21, 22, 29]. In our cases, the ability of LUS in detecting PPE was superior to CXR, detecting it in 35 % vs. 19 % of CAP cases.

LUS is an operator-dependent technique, but expertise can be rapidly achieved by any clinician, provided that initial focused supervised training and adherence to a strict scheme of chest exploration is warranted. Inadequate training and/or incomplete thorax investigation may cause diagnostic pitfalls. In our study, ultrasound scans were not performed by a sole operator, but to ensure reliability of the technique and thus to minimize possible false results, all three paediatricians had achieved a specific expertise through a dedicated course and a practical training (at least 40 LUS investigations done before the beginning of the data collection).

In conclusion, our study further substantiated the previously shown diagnostic accuracy of ultrasound detection of lung consolidations by providing a larger case number and adding clinical and laboratory data in keeping with the diagnosis of pneumonia in febrile children. In the hands of trained clinicians, it may represent a valuable supplemental bedside tool to support the diagnosis of lower respiratory infection and its complications in a paediatric ER setting. Nevertheless, further studies are still needed to ascertain the actual role of LUS in the field of paediatrics, especially focusing on a “lower risk” study population showing milder respiratory involvement and, thus, establishing the negative predictive value of the technique.

Funding source No external funding was secured for this study.

Financial disclosure The authors have no financial relationships relevant to this article to disclose.

Conflict of interest The authors declare that they have no competing interests.

Authors' contributions Mattia Guerra: Dr. Guerra planned and designed the study, performed the data collection, drafted the initial manuscript and approved the final manuscript as submitted.

Giovanni Cricchiutti: Dr. Cricchiutti planned and designed the study, carried out the ultrasound investigations, supervised the data collection, drafted the initial manuscript and approved the final manuscript as submitted.

Paolo Pecile: Dr. Pecile discussed the study design, carried out the ultrasound investigations, reviewed the manuscript and approved the final manuscript as submitted.

Carla Romanello: Dr. Romanello discussed the study design, carried out the ultrasound investigations, reviewed the manuscript and approved the final manuscript as submitted.

Eva Busolini: Dr. Busolini discussed the study design, participated in the initial data collection and approved the final manuscript as submitted.

Francesca Valent: Dr. Valent carried out the statistical analyses, reviewed the manuscript and approved the final manuscript as submitted.

Angelo Rosolen: Prof. Rosolen critically reviewed and revised the study and the manuscript.

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