Lung ultrasound vs chest radiography in the diagnosis of children pneumonia
Systematic evidence
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Abstract
Background: The aim of this meta-analysis was to evaluate the diagnostic value of lung ultrasound (LUS) in comparison to chest radiography (CXR) in children with pneumonia.

Methods: Computer-based retrieval was performed on PubMed and EMBASE. Quality was evaluated according to the quality assessment of diagnostic accuracy studies-2, and Meta-Disc was adopted to perform meta-analysis. Heterogeneity was assessed using Q and $I^2$ statistics. The pooled sensitivity, specificity, and diagnostic odds ratio (DOR) with 95% confidence intervals (CIs) as the primary outcomes were calculated for each index test.

Results: Twenty two studies with a total of 2470 patients met the inclusion criteria. Our results showed that the pooled sensitivity, specificity, and DOR for children with pneumonia diagnosed by LUS were 0.95 (95% CI: 0.94 to 0.96), 0.90 (95% CI: 0.87 to 0.92), and 137.49 (95% CI: 60.21 to 313.98), respectively. The pooled sensitivity, specificity, and DOR for pediatric pneumonia diagnosed by CXR was 0.91 (95% CI: 0.90 to 0.93), 1.00 (95% CI: 0.99 to 1.00), and 369.66 (95% CI: 137.14 to 996.47), respectively. Four clinical signs, including pulmonary consolidation, positive air bronchogram, abnormal pleural line, and pleural effusion were most frequently observed using LUS in the screening of children with pneumonia.

Conclusions: The available evidence suggests that LUS is a reliable, valuable, and alternative method to CXR for the diagnosis of pediatric pneumonia.

Abbreviations: AUC = the areas under curve, CI = confidence interval, CT = Computed Tomography, CXR = chest radiography, DOR = diagnostic odds ratio, FN = false-negative, FP = false-positive, LUS = lung ultrasound, NLP = negative likelihood ratio, PLR = positive likelihood ratio, QUADAS-2 = the quality assessment of diagnostic accuracy studies-2, SROC = the summary receiving operating characteristic, TN = true-negative, TP = true-positive.

Keywords: children, lung, meta-analysis, pneumonia ultrasound

1. Introduction
Pneumonia is a common infectious disease in children and the main cause of death in children.\textsuperscript{[1]} At present, the diagnosis of pneumonia in children mainly depends on medical history, clinical manifestations, and related auxiliary examinations (e.g., chest X-ray), which have played an important role in the diagnosis of pneumonia in children. However, chest radiography (CXR) has several limitations. In detail, the results of CXR are...
greatly affected by internal and external factors such as the child’s posture and reporting physicians. CXR cannot be discerned when lung consolidation is <1.0 cm. This may be due to the fact that chest radiographs are two-dimensional images of normal and abnormal lobes superimposed, making it difficult to observe small lesions. Next, CXR is inconvenient and costly for children to be examined. Additionally, the sensitivity of radiation damage for children is at least 4 times that of adults. Therefore, some scholars are actively exploring and eager to find an inspection method that can not only improve the accuracy of diagnosis of pneumonia, but also reduce exposure to ionizing radiation.

The lung is a gas-containing organ and has always been a blind spot for ultrasound. In recent years, with the continuous advancement of ultrasound diagnostic techniques, ultrasound images have been used to analyze pleural and lung tissue sonograms under pathological conditions. Therefore, it is possible to apply ultrasound to the diagnosis of pneumonia. In 1986, Weinbeg et al initially proposed the use of type B pulmonary ultrasound to evaluate pneumonia. Due to the small size of the lungs in children, changes in the lungs can easily reach the pleura, making it easier to detect abnormal signs during lung ultrasonography. A large number of studies have investigated the diagnostic yield of lung ultrasound (LUS) in children pneumonia. However, these studies not only had wide variation in sample size, but also conveyed inconclusive results. We therefore pre-stated rigorous inclusion criteria and conducted a meta-analysis involving available studies to systematically assess the diagnostic yield of LUS in children with pneumonia.

2. Methods

2.1. Search strategy and selection criteria

Computer-based retrieval was performed on PubMed and EMBASE from inception through October 2019 for eligible studies with the following keywords “ultrasonography” or “ultrasound” and “pneumonia” and “children” or “childhood” or “pediatric”. All eligible trials were published in English. Bibliographies of all potential studies, such as reference lists, citation searches, and relevant systematic reviews, were searched by hand. The present study was supported by the Ethics Committee of Binzhou Medical University Hospital.

The present selection criteria were as follows:
1. population: children or pediatric patients (age < 18 years) with pneumonia based on a combination of clinical data, laboratory results, and CXR;
2. study design: comparing the diagnostic value of LUS vs CXR in the diagnosis of child pneumonia;
3. sufficient data: reported data allowing calculation of the true-positive (TP), false-positive (FP), false-negative (FN), and true-negative (TN) values.

2.2. Data extraction and quality assessment

All data were extracted from all trials by 2 independent investigators (JHY and LP). The data included the first author, publication year, country, number of patients, age and sex of patients, LUS technique and operator, study design, blind, and pneumonia diagnostic criteria. Disagreements among authors were settled by discussion or a third investigator (YBG).

The quality of the studies was evaluated according to the quality assessment of diagnostic accuracy studies-2 (QUADAS-2). The QUADAS-2 tool contains 4 key domains:
1. patient selection,
2. index test,
3. reference standard, and
4. flow and timing.

Each domain is assessed as “yes”, “unclear”, and “no” to judge risk of bias. Furthermore, the first 3 domains are also assessed as “high”, “Unclear”, and “low” concern to judge applicability. We rated the quality assessment and risk of bias using the RevMan 5.3.0 (Nordic Cochrane Centre). This evaluation information is detailed in Supplemental Digital Content (Fig. S1, http://links.lww.com/MD/F370), which is contained in online appendices.

2.3. Statistical analysis

The present study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. The DerSimonian-Laird random-effects model was used to calculate the data as a forest plot of pooled sensitivity, specificity, positive likelihood ratio (PLR) and negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) with 95% confidence intervals (CIs) for LUS and CXR, respectively. The summary receiving operating characteristic (SROC) curve and the pooled diagnostic accuracy (Q* index) as well as the area under curve (AUC) were also measured. The SROC curve move closer to the upper left corner of the larger area under the curve, which indicates that the accuracy of diagnostic tests is higher. Heterogeneity was evaluated using I² statistics, and threshold effect was determined using the Spearman correlation coefficient. If I² > 50%, potential sources of heterogeneity were identified by sensitivity analyses. Furthermore, subgroup analyses were performed to explore observed heterogeneity and examine the influence of various exclusion criteria based on sample sizes (>100 vs ≤100), study design (prospective vs retrospective), blind or non-blind study, LUS operator (expert vs non-expert), and ultrasound probe type (linear vs convex). All meta-analyses were performed using MetaDiSc 1.4 (XI Cochrane Colloquium; Barcelona, Spain). Publication bias was inspected using Deeks funnel plot, which was analyzed using Stata 12.0 (Stata Corporation, College Station, TX, USA). A Z-test was performed to determine whether there was a statistical difference in the overall sensitivity and specificity between LUS and CXR. A two-sided P value of <.05 was considered to indicate statistical significance.

3. Results

3.1. Bibliographic search results

A total of 1605 relevant articles were identified from the initial search. After reviewing the titles and abstracts, 1555 were excluded for duplicate studies and for various reasons (e.g., case reports, editorials, reviews, and or not using both LUS and CXR). A detailed flowchart of the study selection is presented in Figure 1. Finally, the remaining 22 eligible studies with a total of 2470 patients were identified for the present meta-analysis.
3.2. Study characteristics and quality assessment

The main characteristics of the retrieved studies are shown in Table 1. Table 1 shows that the sample size of 22 trials ranged from 47 to 222, and all studies were published between 2008 and 2018. Of all the studies, only 2 studies enrolled neonatal patients, and 3 studies did not report gender situations. In terms of study design, 17 prospective studies and 5 retrospective studies were included in the present study. Next, 19 studies used blind methods and 3 studies used non-blind methods. Furthermore, ultrasonic procedures were performed by experts in 14 studies and by non-experts, including primary or temporary trainers in 8 other studies. Finally, for the type of ultrasound probe, 11 studies used the linear probe, 3 studies used the convex probe, and 8 studies used a linear probe together with a convex probe.

Two authors agreed on each item of the QUADAS-2. The risk-of-bias analyses suggested that 19 trials were followed with low risk in terms of patient selection, index test, reference standard, flow, and timing. Three other studies were followed with a high risk of the index test. In addition, all trials were followed with high concern regarding applicability. The detailed quality assessment of the 22 studies is illustrated in Figure S1, http://links.lww.com/MD/F370.

3.3. Diagnostic accuracy of LUS and CXR

The overall diagnostic sensitivity was 0.95 (95% CI: 0.94 to 0.96; $\chi^2 = 51.89; I^2 = 59.5\%$; $P = .0002$) and 0.91 (95% CI: 0.68 to 0.82; $\chi^2 = 61.49; I^2 = 95.1\%; P = .0000$) (Fig. 2), and the overall diagnostic specificity was 0.90 (95% CI: 0.87 to 0.92; $\chi^2 = 116.76; I^2 = 82\%$) and 1.00 (95% CI: 0.99 to 1.00; $\chi^2 = 16.10; I^2 = 0\%; P = .7640$) (Fig. 3) for children pneumonia diagnosed by LUS and CXR, respectively. Heterogeneity was significant in terms of pooled sensitivity for the 2 arms. Next, sensitivity analyses were performed to further explore the potential source of heterogeneity across studies. Further exclusion of any single study did not resolve the heterogeneity, and the pooled sensitivity ranged from 0.95 (95% CI: 0.94 to 0.96; $\chi^2 = 43.71; I^2 = 54.2\%$) to 0.95 (95% CI: 0.94 to 0.96; $\chi^2 = 51.77$;
## Table 1
Characteristics of randomized controlled trials included in the meta-analysis.

| Author, year | Sample size | Boy/Girl | Mean Age (Range) | Study design | Blinding | Patients setting | LUS operator | Ultrasound system | Pneumonia diagnosis | LUS findings | CXR | TP | FP | FN | TN |
|--------------|-------------|----------|------------------|--------------|----------|-----------------|-------------|-------------------|-------------------|--------------|-----|----|----|----|----|
| Copetti, 2008, Italy | 79 | 37/42 | 5.1y (6 mo-16 y) | Prospective | Yes | Emergency Department | The same expert operator | Esaote, convex probe (3.5-5 MHz), linear probe (7.5-10 MHz) | CXR | LUS 60 | 0 | 0 | 19 |
| Iuri, 2009, Italy | 28 | 17/11 | 4.5y (4mo-17y) | Prospective | Yes | Paediatric emergency ward | Two radiologists | Philips, convex probe (2-5 MHz) and linear probe (5-12MHz) | CXR | LUS 53 | 7 | 19 | 22 | 2 | 4 |
| Caiulo, 2013, Italy | 102 | 53/49 | 5y (1-16y) | Prospective | Yes | Pediatric department | An expert pediatric sonographer | Sonosite, GS60, Siemensa, linear probe (7.5-10MHz) | Physical and CXR | LUS 88 | 8 | 13 | 31 | 5 | 8 |
| Shah, 2013, American | 200 | 112/88 | 3y (1-8y) | Prospective | Yes | Emergency departments | Trained clinicians | MyLab, convex probe (2.5-6.6MHz), linear probe (7.5-12MHz) | Physical and CR | LUS 24 | 0 | 0 | 164 | 68 | 0 | 7 |
| Hadeel, 2013, Egypt | 75 | 36/39 | 3-26d | Prospective | NO | NICU | The same radiologist | Nemio XG SSA-590A, and a linear 7MHz | Physical and CR | LUS 48 | 0 | 0 | 55 | 159 | 4 | 0 |
| Esposito, 2014, Italy | 103 | 56/47 | 5.6y (1mo-14y) | Prospective | Yes | Pediatric ICU | Trained resident paediatrics | MyLab, convex probe (2.5-6.6MHz), linear probe (7.5-12MHz) | Physical and CR | LUS 151 | 12 | 0 | 40 | 40 | 0 | 40 |
| Ho, 2014, Taiwan | 163 | 91/72 | 6.1y | Retrospective | Yes | Pediatric ward | Experienced pediatric pulmonologists | SonoS57500, Philips, convex probe (5MHz) | BTS guideline | LUS 151 | 0 | 0 | 0 | 40 | 0 | 40 |
| Liu, 2014, China | 80 | 43/37 | Newborn | Prospective | Yes | Department of Neonatology & NICU | A single examiner expert physician | GE Voluson E5 or E8, linear probe (9-12MHz) | Physical and CXR | LUS 88 | 8 | 13 | 31 | 5 | 5 |
| Reali, 2014, Italy | 107 | 61/46 | 4y (0-16y) | Prospective | Yes | Pediatric department | A pulmonologist and two residents | Mylab25; Esaote, Genoa and a linear probe (7.5-10MHz) | Physical and CXR | LUS 66 | 2 | 15 | 4 | 22 | 25 | 1 | 4 | 22 |
| Iorio, 2015, Italy | 52 | NR | 3.5y (2-12.5y) | Retrospective | Yes | Pediatric ward | The same expert operator | SonoSite, linear probe (5-10MHz) | BTS guideline | LUS 147 | 0 | 7 | 0 |
| Dianova, 2015, Russia | 154 | 87/67 | 0-18y | Prospective | Yes | Children’s Teaching Hospital | Enerpamed radiologist | Hitachi Vision Avius (Japan) and sonoscope s8Ep (China) with 4-11 MHz multifrequency linear probes and 4-11 MHz convex probes | Clinical, CR, CT | LUS 126 | 0 | 28 | 0 | 0 | 28 |
| Urbankowska, 2015, Poland | 106 | NR | 52.5mo (1-213mo) | Prospective | Yes | Pediatric ward | The same pediatric sonographer | ALOKA, linear probe (3-7and5-9MHz) | Physical and CR | LUS 71 | 0 | 5 | 30 | 30 | 0 | 5 | 30 | 30 |

(continued)
### Table 1 (continued)

| Author, year | Sample size | MeanAge (Range) | Study design | Blinding | Patients setting | LUS operator | Ultrasound system | Pneumonia diagnosis | LUS findings |
|--------------|-------------|-----------------|--------------|----------|-----------------|--------------|-------------------|---------------------|--------------|
| Guerra, 2016, Italy | 222 | 3mo-16y | Prospective | Yes | Paediatric department | Three paediatricians with specific LUS expertise | MyLAB25, Esaote, linear probe (7.5–10 MHz), convex probe (3.5–6 MHz) | Clinical characteristics | Consolidations |
| Ianniello, 2016, Italy | 84 | 6y (3–16y) | Retrospective | No | Emergency department | Professional sonographer | Siemens, convex probe 4 MHz and linear probe (7.5–10 MHz) | Clinical, CPR | CONSOLIDATIONS |
| Samson, 2016, Spain | 200 | 29.5mo (18.5–52.5mo) | Prospective | Yes | Emergency department | Paediatricians with limited training | Sonostar, linear probe (6–15 MHz) | Physical and CPR | CONSOLIDATIONS |
| Boursian, 2017, Greece | 69 | 6mo-12y | Prospective | Yes | Emergency department | Experienced pediatric radiologist | Microconvex probe (5–8 MHz), linear probe (5–12 MHz), convex (3–6 MHz) | Clinical criteria and CPR | CONSOLIDATIONS |
| Man, 2017, Romania | 81 | 6.5y | Retrospective | No | Emergency department | Senior radiologist experienced | Accuvix V20, convex probe (7–11 MHz) and linear probe (3.5–5 MHz) | CPR | CONSOLIDATIONS |
| Gaaes, 2017, Belgium | 143 | 41mo (8d–14y) | Prospective | Yes | Emergency room | Basic ultrasound knowledge | Philips IU-22, linear probe (12–6 MHz) | CPR | CONSOLIDATIONS |
| Yilmaz, 2017, Turkey | 160 | 1mo–18y | Prospective | Yes | Pediatric emergency department | A single trained operator | SonoSite, linear probe (6–13 MHz) | BTS guideline | Pleural irregularity, consolidation, FBL, PE, air bronchograms |
| Yadav, 2017, India | 118 | 26.22mo (2–59 mo) | Prospective | Yes | Pediatric emergency department | Trained pulmonary radiologist | GE, LOGIQ P5, microconvex | Physical and CPR | CONSOLIDATIONS |
| Iorio, 2018, Italy | 47 | 4y (1mo-12y) | Retrospective | Yes | Pediatric department | A skilled sonographer | Sonosite MicroMax Systems, geceographic equipment with a 5–to10 MHz linear probe (L38e) | Medical records | CONSOLIDATIONS |
| Lissaman, 2018, Australia | 97 | 1 mo to 18y | Prospective | Yes | Pediatric emergency department | A first-year paediatric emergency medicine fellow with specific training | A Zonare z.one ultrasound using an L14–5w linear transducer | CPR | CONSOLIDATIONS |

**Note:** BTS = British Thoracic Society, CPR = chest radiography, ED = emergency department, FBL = focal B-linse, FN = false-negative, FP = false-positive, ICU = intensive care unit, LUS = lung ultrasound, NICU = newborn intensive care unit, PE = pleural effusion, PLA = pleural line abnormality, TN = true-negative, TP = true-positive.
Next, threshold effect analysis showed that the Spearman's correlation coefficients were $-0.390 (P = .073)$ and $-0.421 (P = .051)$ for LUS and CXR, which suggested that no diagnostic threshold effect existed for pneumonia diagnoses. Moreover, the heterogeneity among studies could mainly result from clinical and methodological differences.

The pooled PLR, NLR, and DOR were 8.67 (95% CI: 3.98 to 18.89), 0.07 (95% CI: 0.05 to 0.10), and 137.49 (95% CI: 60.21 to 313.98) for LUS, respectively. Correspondingly, the pooled PLR, NLR, and DOR were 19.96 (95% CI: 10.42 to 38.24), 0.09 (95% CI: 0.06 to 0.14), and 369.66 (95% CI: 137.14 to 996.47) for CXR, respectively. The above results are detailed in the Supplemental Digital Content (Fig. S2, http://links.lww.com/MD/F372, Fig. S3, http://links.lww.com/MD/F373, and Fig. S4, http://links.lww.com/MD/F375). Additionally, the 2 SROC curves are presented in Figure 4, which shows that the AUC and $Q^*$ index with a standard error (SE) of 0.9817 (0.9405 ± 0.0122) and 0.9866 (0.9505 ± 0.0125) for LUS and CXR (Fig. 5), respectively.

Specifically, the Z-test for the overall sensitivity and specificity suggested that there was no statistical difference between LUS and CXR (all $P > .05$). In other words, LUS and CXR have similar sensitivity and specificity.

### 3.4. Subgroup analyses

We performed subgroup analyses using a random effects model to explore the heterogeneity of sensitivity and examine the influence of various exclusion criteria based on sample sizes
(>100 vs ≤100), study design (prospective vs. retrospective), blind or non-blind study, LUS operator (expert vs non-expert), and ultrasound probe type (linear vs convex). Table 2 shows the detailed indication for subgroup analyses of LUS and CXR for the pooled sensitivity, specificity, and DOR in all eligible studies.

3.5. Publication bias

Deeks funnel plot asymmetry test was used to evaluate the final set of studies for potential publication bias. The slope coefficient was associated with a $P$ value of .70, which suggested symmetry in the data and no publication bias (Fig. 5).
4. Discussion

The current meta-analysis including 22 studies was conducted to systematically evaluate the diagnostic value of LUS in comparison to CXR in children with pneumonia. Our results indicate that LUS is a reliable, valuable, and alternative method to CXR and could be considered as a first-line imaging modality for the diagnosis of pediatric pneumonia.

To date, several systematic reviews and meta-analyses have investigated the diagnostic value of LUS in children pneumonia. However, these meta-analyses only described data on LUS, unilaterally analyzed the diagnostic value of LUS, and did not analyze the diagnostic value of CXR for children with pneumonia. From this point of view, the above meta-analyses did not systematically compare the diagnostic value of LUS and CXR, and they were also limited in the literature. Considering the above limitations, we carried out the present meta-analysis combining existing studies to increase the sample size, strengthen our analyses, and produce more robust results to compare the diagnostic value of LUS in comparison to CXR in children with pneumonia.

In the present study, we mainly focused on evaluating the diagnostic value of LUS in comparison to CXR in pediatric pneumonia. Our results showed that the pooled sensitivity was 0.95, 0.91, specificity was 0.90, and 1.00, DOR was 137.49 and 369.66, and AUC was 0.9817 and 0.9866 for LUS and CXR, respectively. The Z-test results suggested that there was no statistical difference in the pooled sensitivity and specificity between LUS and CXR (all \( P > 0.05 \)), which suggested that the sensitivity and specificity of LUS were not inferior to those of CXR. Additionally, the 2 SROCs of LUS and CXR are presented in Figure 4, which suggests that both LUS and CXR have a fairly high diagnostic accuracy. Next, our sensitivity analyses did not significantly alter the heterogeneity among studies for pooled sensitivity. Threshold effect analysis showed that no diagnostic threshold effect existed for pneumonia diagnoses, which indicated that the heterogeneity among studies could be seen as a result of clinical and methodological differences. Moreover, the results of subgroup analyses indicated that LUS may appear to be slightly higher than CXR, but the difference was not statistically significant. Overall, those prospective blind studies with expert operators should be more specific for LUS. It should be noted that an ultrasound convex probe helps to improve the sensitivity and specificity of LUS diagnosis in pediatric pneumonia. However, more studies are needed to investigate these topics of interest. Finally, 4 clinical signs, including pulmonary consolidation, positive air bronchogram, abnormal pleural line, and pleural effusion, were most frequently observed using LUS in the screening of children pneumonia. Further research should focus on these diagnostic signs of LUS for pediatric pneumonia.

To be sure, there were several limitations to our study. First, the child patients were heterogeneous with different regions, different ages, and sex ratios. The experience of LUS operators was not consistent and may interfere with the accuracy of pneumonia diagnosis. Second, the design of the study was different, including blind methods and prospective or retrospective studies. The ultrasound system was not consistent and may interfere with the LUS operators judgment. Third, the sample size was different, and some studies with a wide variation in sample size were incorporated into our analysis. Overestimation of the diagnostic value is most likely to occur in smaller than in larger studies.
Finally, several unpublished or missing data may increase the risk of bias.

5. Conclusions
In summary, our results suggest that LUS is a reliable, valuable, and alternative tool to CXR for children with suspected pneumonia, and LUS should be considered as a first-line imaging modality for the diagnosis of pediatric pneumonia. However, considering the significant heterogeneity found across the individual studies, further more methodologically rigorous studies are needed to focus on the diagnostic accuracy of LUS in pediatric pneumonia.

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