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Ana Alexandra Monteiro Rainho Governo Ribeiro

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Autora

Ana Alexandra Monteiro Rainho Governo Ribeiro

ana.alex.governo@gmail.com

Mestrado Integrado em Medicina

Instituto de Ciências Biomédicas Abel Salazar

Orientação

Professor Doutor Manuel José Ferreira de Magalhães

ferreirademagalhaes@gmail.com

Centro Hospitalar Universitário de Santo António, Portugal

Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto

CINTESIS/MEDICDS - Faculdade de Medicina, Universidade do Porto

Coorientação

Dr.ª Sara Alexandra Pinheiro Monteiro

saraapmonteiro@gmail.com

Centro Hospitalar Universitário de Santo António, Portugal

Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto

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Autora | Ana Alexandra Monteiro Rainho Governo Ribeiro

Assinado por: **MANUEL JOSÉ FERREIRA DE MAGALHÃES**
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Resumo

Introdução e Objetivos

Cada vez mais evidências sugerem que a ecografia pulmonar (LUS) é uma ferramenta poderosa na síndrome de dificuldade respiratória neonatal (NRDS). O principal objetivo desta revisão sistemática foi compilar a literatura que reconhece o uso da LUS na NRDS.

Metodologia

Dois investigadores independentes pesquisaram as bases de dados Pubmed®, Scopus® e Cochrane® Centre Register of Controlled Trials (CENTRAL) e selecionaram os estudos que respondiam aos critérios de inclusão. A estratégia de pesquisa incluiu a *query* (Respiratory Distress Syndrome, Newborn[MeSH Terms]) AND ((ultrasound[MeSH Terms]) OR ("Lung/diagnostic imaging"[MeSH])) AND (Infant, Newborn[MeSH Terms]). Um terceiro investigador teve a decisão final na inclusão dos artigos em caso de discordância. Após a avaliação da qualidade dos artigos (QUADAS-2), foram avaliadas as características psicométricas de cada medida/instrumento.

Resultados

O valor diagnóstico da LUS foi avaliado em 11 artigos, enquanto 4 avaliaram como o uso da LUS interfere na escolha do método terapêutico e 4 avaliaram o valor prognóstico. A sensibilidade e especificidade diagnósticas tiveram valores de 71,4% a 100% e 92% a 100%, respetivamente. Já na terapêutica, a LUS teve impacto na apreciação dos níveis de aeração para avaliar se seria necessária terapia com surfactante ou ventilação mecânica (MV) e qual o nível ideal de Pressão Expiratória Final Positiva (PEEP). Em termos prognósticos, verificou-se que a LUS pode prever o desenvolvimento de Displasia Broncopulmonar (DBP), a necessidade de MV ou de terapia com surfactante.

Conclusões

A LUS é um método promissor, fiável, barato, repetível e não ionizante, que pode ser realizado à beira do leito. As evidências atuais apoiam a LUS como uma ferramenta útil no diagnóstico, avaliação terapêutica e prognóstica da NRDS.

Abstract

Introduction and Objectives

Increasing evidence suggests lung ultrasound (LUS) is a powerful tool in neonatal respiratory distress syndrome (NRDS). This systematic review's main aim was to compile literature that acknowledges the use of LUS in NRDS.

Methods

Two independent researchers searched Pubmed®, Scopus® and Cochrane® Centre Register of Controlled Trials (CENTRAL) databases and selected the studies that fit the inclusion criteria. The research strategy included the query (Respiratory Distress Syndrome, Newborn[MeSH Terms]) AND ((ultrasound[MeSH Terms]) OR ("Lung/diagnostic imaging"[MeSH])) AND (Infant, Newborn[MeSH Terms]). A third investigator decided on the inclusion of the articles in case of disagreement. Later, after evaluation of the quality of the articles (QUADAS-2), the psychometric characteristics were evaluated.

Results

The diagnostic value of LUS was evaluated in 11 of them, whilst 4 assessed how the use of LUS interfered with choosing the therapeutic method and 4 evaluated the prognostic value. The diagnostic sensitivity and specificity had values from 71,4% to 100% and 92% to 100%, respectively. In the therapeutic sense, LUS had an impact in evaluating the aeration levels to address if surfactant therapy and mechanical ventilation (MV) might be needed, and the optimal positive end-expiratory pressure (PEEP) level. Prognostically, it was found that LUS can predict the development of Bronchopulmonary Dysplasia (BPD), the need for MV or surfactant therapy.

Conclusion

LUS is a promising method that is reliable, inexpensive, repeatable and nonionizing, which can be performed at the bedside. Current evidence supports LUS as a useful tool in the diagnostic, therapeutic and prognostic management of NRDS.

List of Abbreviations

BPD: Bronchopulmonary Dysplasia

CPAP: Continuous Positive Airway Pressure

CS: Caesarean Section

CXR: Chest Radiography

DOL: Day of Life

GA: Gestational Age

LUS: Lung Ultrasound

MV: Mechanical Ventilation

NICU: Neonatal Intensive Care Unit

NRDS: Respiratory Distress Syndrome

TTN: Transient Tachypnea of the Newborn

PEEP: Positive End-Expiratory Pressure

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Introduction

One of the most prevalent diseases in newborn, is neonatal respiratory distress syndrome (NRDS). This disorder is mostly caused by pulmonary surfactant deficiency at birth, which explains the high prevalence in preterm newborns.[1] The lack of surfactant leads to atelectasis and alveoli collapse shortly after birth making this one of the most important causes of morbidity in the neonatal intensive care unit (NICU). The clinical presentation of NRDS is tachypnea, nasal flaring, expiratory grunting, chest retractions, and central cyanosis.[2] It is also known that the risk increases with decreasing gestational age (GA), with a calculated incidence of about 92% in newborns with a GA of 24-25 weeks, 88% at 26-27 weeks, 76% at 28-29 weeks and 57% at 30-31 weeks.[3]

It is of extreme importance to make an early diagnosis to optimize the treatment and prevent the progression of the disease, which is the main cause of neonatal death.[4,5] At the moment the leading tool to establish a diagnosis is a chest radiography (CXR) combined with the clinical findings and blood gases results.[6,7] However, exposing a neonate to ionizing radiation has a significantly increased potential for negative effects.[8,9] Those who are exposed early in life have a higher relative risk of cancers throughout life.[10]

Therefore, a need to find a less harmful diagnostic test has risen and thirty years ago lung ultrasound (LUS) was first used with the purpose of diagnosing NRDS.[11,12] LUS has many advantages over CXR since it's non-ionizing, ready-to-use, and reproducible. Moreover, in recent years, several publications have showed that it is a feasible and accurate tool for diagnosing most newborn lung diseases such as pneumonia, transient tachypnea of the newborn (TTN) and NRDS.[13,14]

LUS has also been demonstrated to have the ability to predict CPAP failure[15,16] and guide surfactant replacement.[17] Its efficiency in diagnosing the complications of NRDS, such as pneumonia, atelectasis or hemorrhage,[18] and how it might evolve has also been proven through the years.[19]

It's becoming clearer that this could be a method for screening and diagnosing NRDS, with less long-term effects. The way it can be reproduced through time may make this a useful tool for monitoring. So, the main aim of this systematic review is to compile literature that acknowledges the use of lung ultrasound in NRDS and understanding in which way is it useful in a NICU environment.

Methods

Information Sources

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[20] We searched the entries in PubMed, SCOPUS and Cochrane Centre Register of Controlled Trials databases. The search query was (Respiratory Distress Syndrome, Newborn[MeSH Terms]) AND ((ultrasound[MeSH Terms]) OR ("Lung/diagnostic imaging"[MeSH])) AND (Infant, Newborn[MeSH Terms]).

Eligibility Criteria

All clinical studies published before May 2023 about NRDS (under 28 days of age) and in all languages were considered for eligibility.

Inclusion Criteria

For inclusion in this systematic review, we considered cohort or case-control studies that used LUS as a tool for NRDS considering 3 main domains: diagnostic, therapeutic and prognostic. The studies needed to have been conducted in human newborns (under 28 days of age at recruitment).

Exclusion Criteria

Reviews or other secondary studies were excluded. Also, duplicated studies and conference abstracts were rejected.

Search Strategy

Firstly, all the titles and abstracts identified as potentially eligible were independently read by two different researchers (AR and SM) for selecting studies based on inclusion and exclusion criteria. Any disagreements between individual judgements were solved by a third researcher (MFM). Then, the full-text articles were read to decide which ones were a part of the final review, according to inclusion criteria. The citation pool was further supplemented from manual assessment of the reference lists of the retrieved articles and from other publications identified as being relevant for further review.

Data Collection Process

Data was extracted and checked by two researchers (AR and SM) and disagreements between individual judgements were resolved by the third investigator (MFM), that made the final decision. For the data extraction, information about the participants' gestational age, LUS use, associated diseases, study design, settings, the methodology, and results were included.

Quality Assessment

For the studies included, their methodological quality was assessed by two researchers (AG and SM) using the QUADAS-2 grid (Fig. 1).[21]

Results

Study Selection

A total of 772 articles were identified in PubMed (n = 768), Scopus (n = 4) and Cochrane Centre Register of Controlled Trials (n = 0). From these, 749 were excluded from the title and 33 had their abstract assessed, resulting in the exclusion of 10 for being systematic reviews and 6 for being comments to the editor. After full-text eligibility evaluation, 17 studies met the inclusion criteria (Fig.2). The diagnostic value of LUS was evaluated in 11 of them,[18,19,22-30] whilst 4 assessed how the use of LUS interfered when choosing the best therapeutic method[31-34] and 4 evaluated the prognostic value.[28,30,35,36]

Characteristics of the Included Studies

As seen in Table I, the 17 studies included were published between 2006 and 2022, all of them written in English. All the included studies were prospective, 3 case-control[19,24,25] and 14 cohort.[18,22,23,26-36] 15 were single-center and 2 were multicentric. Three of them were conducted in Asia,[25,28,33] one in Northern Africa[24] and the rest in Europe,[18,19,22,23,26,27,29-32,34-36] mostly in Italy (6)[19,23,26,29,31,35].

LUS approach, classification and scoring system

The approach technique that was mostly used was transthoracic (14 studies). However, there were small differences between approach criteria, 2 of them used both transthoracic and transabdominal views[18,25], while only one focused exclusively on the transabdominal method.[22] Four studies used the score validated by Brat et al.,[15,30,31,34,35] and others used a modified Brat score: Pang et al.[28] used 12 scanned areas, Gregorio-Hernández et al.[32] used different score grades, and others used mixed changes (Szymański et al.[36] – lateral zone to posterior and 5 grades; Jiang et al.[33] - 14 areas and 6 grades). Poerio et al.[29] used a different classification, according to the general appearance of the lung (Type 1, Type 2 and Type 3). All others used a LUS pattern to identify NRDS, with no scoring system added.[18,19,22-27]

Study Purpose: diagnosis, therapeutic and prognosis

From the 11 studies that assessed the diagnostic accuracy of LUS, 9 assessed the accuracy in diagnosing NRDS [19,22,23,25-30] and 2 the accuracy in diagnosing complications of NRDS.[18,24] In NRDS diagnosis, the estimated specificity and sensitivity ranged from 92.0 to 100 and 71.4 to 100, respectively. Five of them had 100% specificity (4 studies with transthoracic view and 1 with transabdominal plus transthoracic view).[19,25-27,29] Regarding sensitivity, 3 studies

had an estimated value of 100%,[19,22,27] with 1 of the studies using an exclusive transabdominal view[22] while the others only focused on the transthoracic approach. When evaluating the accuracy in diagnosing complications of NRDS, Lovrenski et al. found a high correlation with CXR, having an almost perfect match in 98% (pneumonia, atelectasis, hemorrhage) and 2% of false negatives (partial pneumothorax).[18] Sawires et al. corroborated this information by also finding that LUS was superior to CXR in the detection of consolidation and sub-pleural atelectasis, but less reliable in the detection of pneumothorax.[24]

When evaluating the therapeutic implications of LUS, this tool was found to have a high accuracy to assess newborns who might benefit for surfactant treatment (sensitivity of 86% and specificity of 88%).[31] Also, Jiang et al. published a scoring system to predict the risk of withdrawal failure of Mechanical Ventilation (MV), with sensitivity of 92.4% and specificity of 93.8%.[33] An increased advantage of LUS was also observed in finding the optimal positive end-expiratory pressure (PEEP) level according to the aeration level visualized.[34] Gregorio-Hernández et al. had also demonstrated that the changes in aeration arrive before the increase in FiO2, which was linked to a better understanding of the need for surfactant or MV.[32]

The prognostic value was also assessed by Raimondi et al. in infants with GA of 28-30 weeks; LUS higher scores in the first 24 hours of life predicted higher incidence of BPD at 7 days of life (sensitivity of 78% and specificity of 87%).[35] Vardar et al. has shown that a cut-off LUS score of 4 predicted the need for surfactant with 96% sensitivity and 100% specificity, while a LUS score of 9 predicted Continuous Positive Airway Pressure (CPAP) failure.[30] Meanwhile, the postnatal (first 24 hours) LUS score has a significant predictive ability for the need for MV at 3rd day of life, according to Szymański et al.,[36] which was also supported by Pang et al., following the analysis of the consolidation area. [28]

Gestational age subgroups

Most of the studies targeted preterm infants, except Poerio et al. and Rodriguez-Fanjul et al.[29,34] There were 6 that evaluated the diagnostic value,[19,22,23,25-27] 7 for the prognostic[18,24,28,30,32,35,36] and 2 for the therapeutic purposes.[31,33] Raimondi et al. had 3 cohorts divided by GA, 25-27, 28-30 and 31-33, that, during the analysis, demonstrated the capacity that LUS performed on the seventh day had of predicting BPD in GA from 25 to 30 weeks.[35]Rodriguez-Fanjul et al. studied purely term neonates finding that LUS was a useful tool in the evaluation of therapeutic success since it helped calculate the optimal PEEP level by seeing in real time the pulmonary aeration with LUS.[34] Poerio et al. also focused solely on late preterm and term infants born via caesarean section, finding that LUS performed in the first 30 min of life had a specificity of 100% and sensitivity of 71.4% for NRDS and need to NICU admission.[29]

Discussion

This systematic review showed that LUS is a useful tool in the diagnosis, in the therapeutic management and in the prognosis evaluation of neonates with NRDS. Till date, there were identified 17 original studies assessing this LUS applicability (3 case-control[19,24,25] and 14 prospective studies [18,22,23,26-36]).

LUS is already a disseminated tool in most of the critical care adult centers,[37] and it is an important diagnostic tool in some guidelines.[38]

Several authors have been keen to pursue the importance to apply on clinical grounds what our systematic review showed. Specifically, the need to use some tool that is less arming to the neonate than CXR is reinforced, while also being reliable, quick, repeatable, easy-to-use and highly performative, to act as soon as possible to prevent further damage is being demonstrated.[39] Current guidelines, in line with new data, reinforces that CXR may be an unreliable and delayed resource for guiding NRDS therapy, since there is no consensus in criteria to guide surfactant or CPAP therapy.[40] In fact, Perri et al. showed that LUS had better accuracy for recognition of those newborn requiring surfactant treatment when compared with CXR (sensitivity: LUS 86% vs CXR 82%; specificity: LUS 88% vs CXR 76%).[31]

Therefore, the studies analyzed in this review consolidate this information by showing there is a much more effective way to diagnose NRDS while also doing its follow-up and assessing the therapeutic efficacy and prognostic value.

The most common LUS score is the one validated by Brat et al., also the one used in 4 of the studies included in this review.[15] It divides the lungs into 3 areas (anterior upper and lower, and lateral) with a 4-grading system (0 = A-pattern; 1= B-pattern, ≥3 well-spaced B-lines; 2= severe B-pattern, crowded and coalescent B-lines; 3= extensive consolidation), its use was proven to be helpful in finding if the therapeutic applied was making any difference in the improvement of the neonate,[30,31,34] also having a role in the prediction of BPD as a major complication associated with NRDS.[35] The other modified scores are also important in the sense that complement those findings. For instance, Pang et al., Szymanski and Jiang, included the posterior fields, instead of lateral, with the underlying rational that consolidations may be located in the posterior areas of the lung, following the gravitational pool in a newborn that is mostly in dorsal decubitus.[28,33,36]

The number of assessed lung sites was also different. Pang et al. used 12 and Jiang et al. 14, which encapsulates more lung areas assessed when compared to Brat et al. This is still a issue of debate since fewer scanned areas may be easier to implement because of the small size of the neonate thorax.[28,33]

The scoring systems was also heterogenic, with some authors giving more or less points in each scanned area according to slight differences in the appearance of the lung.[33,36] For instance, the simplified version of the scoring system used by Poerio et al. has the lowest sensitivity of all studies (71.4%), which might be due to the lack of accuracy inherent to a more simplistic way of evaluating the parenchyma. [29]It would be important to have some consensus on the scoring system approach in order to adopt it in future guidelines.

Looking to the different LUS approaches, Copetti et al. claimed that, when compared with the transabdominal approach, the transthoracic view could examine all the lung fields rather than only the base.[19] This report might have had a clinical and research impact since following this manuscript, in 2008, all the studies that used transabdominal view have associated also the transthoracic view.[18,25]

In the last four years, the purpose of the studies has also shifted. In the recent years, the studies were more directed towards finding the value in prognosis[35,36] and in therapeutic effect.[33,34] This might be a response to the way LUS has been constantly scoring high in specificity and sensitivity when diagnosing NRDS. [19,25-27,29] Another information perceived when examining the data was that there is a lack of studies that assessed the accuracy of LUS in the assessment of late preterm and term neonates. Even though the lack of studies might be due to the lower incidence of NRDS with increased GA,[41] it would be important to have a more knowledgeable understanding of how LUS performs in all GA. This is also important when noticed that the study that had the lowest sensitivity was precisely Poerio et al., the one that have focused on newborns with GA higher than 34 weeks, with 71.4% against all other studies that have values above 95%.[29]

LUS has come a long way since the first time it was thought that it could become an essential tool in NRDS management. Still, there is room for improvement by having more studies that include those who have congenital malformation, structural heart disease or chromosomal diseases/syndromes, since these were largely left out in most of the papers.

Conclusions

LUS is an accurate tool for NRDS, specifically, with applicability in diagnosis, evaluation of therapeutic management, prediction of complications or prognosis of future evolvement. Its benefits, when in comparison to CXR, are being a low-cost, non-ionizing and repeatable method that can be performed at the bedside. However, it is important to note that this conclusion is based on a small and heterogenic number of studies. It would be of most importance to invest in more multicenter studies and in studies with more late term and term newborns to assess the full capacity of LUS in NRDS.

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Appendix

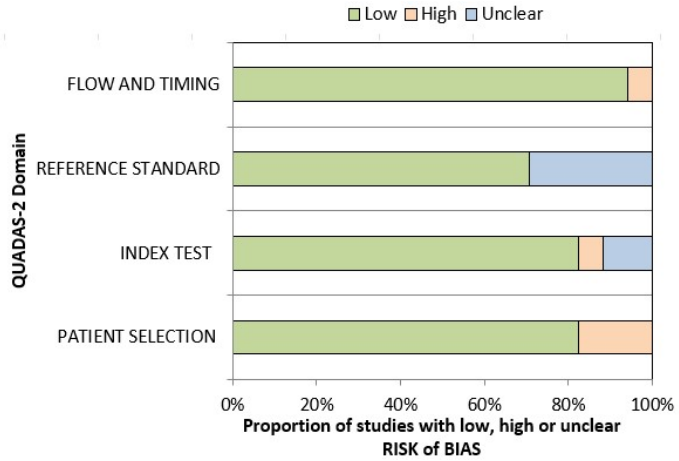

Figure 1. *QUADAS - 2 Risk of Bias Evaluation*

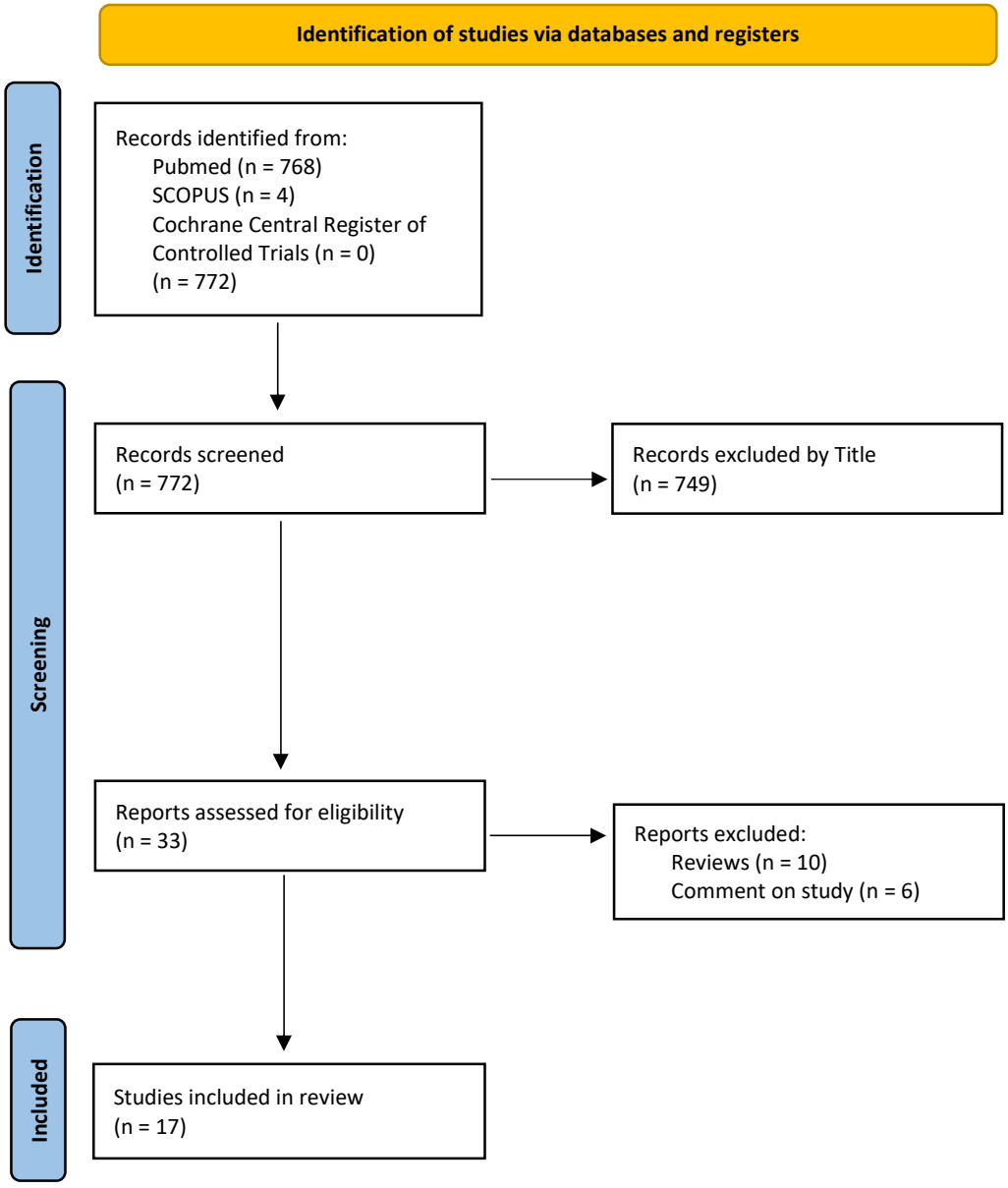

Figure 2*. Flow diagram. Results of the literature search and selection.*

Table I. *Results - Lung Ultrasound use in Neonatal Respiratory Distress Syndrome*

Study	Year	Origin	Study Type	Sample Size	GA (weeks)	LUS Technique	LUS Criteria	Study Purpose			Limitations
								Diagnosis	Therapeutic	Prognosis	
Bober et al.[22]	2006	Poland	Prospective, cohort	131	32.0 ± 4.4 <34 (61,8%) 37-37 (19,8%) >37 (18,4%)	Transabdominal	Retrophrenic hyperechogenicity with B lines diverging radially.	The transabdominal ultrasound examination has 100% sensitivity and 92% specificity in NRDS.			There was no information about treatment before LUS. Only accounted for alterations on the lung bases. It was also **monocentric**.
Copetti et al.[19]	2008	Italy	Prospective, case-control	55	27.2 ± 2.7	Transthoracic	Bi-lateral white lung, absence of spared areas, thickened and irregular pleural line.	The sensitivity and specificity were 100% for NRDS.			The small sample size, the ultrasound operator was not blinded to the clinical history and radiological findings.
Lovrenski et al.[18]	2012	Serbia	Prospective, cohort	47	30.9 ± 3.2	Transthoracic + Transabdominal	Consolidation, air bronchograms and B-Lines, anterior, posterior, and lateral lung areas with transhepatic/splenic for both lung bases.	Detection of complications (pneumonia, hemorrhage, and atelectasis) in preterm infants with NRDS with the same accuracy as CXRs.			The investigator who evaluated the LUS was the same one that evaluated clinical and CXR findings, the **monocentric** design of the study.
Vergine et al.[23]	2014	Italy	Prospective, cohort	59	33 ± 4.0 4 cohorts < 24 (4%) 24-26 (13%) 27-29 (17%) 30-32 (39%) 33-35 (23%) >35 (4%)	Transthoracic	Bi-lateral white lung, coalescent B-lines with thickened and irregular pleural line.	A sensitivity of 95,6% and a specificity of 94,4% for NRDS, in the first hour of admission.			The small sample size and only NRDS and TTN were evaluated, the **monocentric** design of the study.
Sawires et al.[24]	2015	Egypt	Prospective, case-control	130	29.9 ± 1.3	Transthoracic	A thickened and irregular pleural line with a small sub-pleural patch of consolidation, scattered echogenic air bronchogram.	LUS is a good alternative to CXR in the detection of complications of NRDS, as consolidations, atelectasis. and micro-abscesses.			There was no comparison with other causes of respiratory distress, such as pneumonia or TTN, being a **monocentric** study.

Rachuri et al.[25]	2017	India	Prospective, case-control	63	34.5 ± 3.2	Transthoracic + Transabdominal	**Trans-thoracic -** Bilateral white lung absence of spared areas, thickened and irregular pleural line. **Trans-abdominal -** Diffuse retro-diaphragmatic hyper-echogenicity.	The sensitivity and specificity of transthoracic LUS were 98.4% and 100%, respectively. Via transabdominal, all infants with NRDS had diffuse echogenicity.		Failure to include more infants with other etiologies for comparison such as pneumonia and pneumothorax, small sample size, and the **monocentric** design of the study.
Perri et al.[31]	2018	Italy	Prospective, cohort	67	mean of 31.0 GA ≤ 30 (48%) 30 < GA > 33 (41%) GA ≥ 33 (11%)	Transthoracic	Brat et al score with its 4-grading system* (0,1,2,3)		Recognition of those who might need surfactant with a sensitivity of 86% and specificity of 88% vs CXR with 82% and 76%.	The small sample size and the **monocentric** design of the study.
Corsini et al.[26]	2018	Italy	Prospective, cohort	124	overall, 33.0 ± 5.0 preterm 30.0 ± 1.0 (57%) late preterm 36.0 ± 1.0 (14%) term 39.0 ± 3.0 (29%)	Transthoracic	Bilateral sign of abnormalities of the pleural line (thickened and irregular pleural line), white lung image and absence of spared area in all lung fields.	The concordance between LUS and CXR diagnosis was 91%, with a shorter time to diagnose with LUS (≈ 9,5 min), in the first 24 hours of life. Sensitivity of 96,7% and specificity of 100%.		The small sample size and the **monocentric** design of the study.
Grimaldi et al.[27]	2019	France	Prospective, cohort	52	mean of 33 (25–41) preterm 25-37 (77%) full term 37-41 (23%)	Transthoracic	Diffuse alveolo-interstitial syndrome with compact B-lines or global hyper echogenicity, irregular pleural line with small subpleural hyperechoic abnormalities or consolidations.	Sensitivity and specificity in diagnosis accuracy for NRDS was 100%, the same value was calculated for TTN, pneumomediastinum and meconium aspiration syndrome.		The small sample size, only one radiologist was analyzing the LUS, and there was a big-time difference between the CXR and the LUS, which may have caused a delay on the performance.

Pang et al.[28]	2019	China	Prospective, cohort	146	29 ± 3.4	Transthoracic	Modified LUS score with 12 areas, 6 for each lung (upper and lower areas of anterior, posterior, and lateral sections), and the same 4-grading system* as Brat et al.	The LUS score and consolidation areas can discriminate NRDS from non-NRDS and the different NRDS grades.		LUS can predict the need for MV, according to the consolidation area.	The small sample size, the consistency and time of LUS image analysis were not evaluated, there was a discrepancy between the GA of those with NRDS and the TTN ones, being a **monocentric** study.
Gregorio-Hernández et al.[32]	2019	Spain	Prospective, cohort	128	29 ± 3.0	Transthoracic	A score based on Brat et al, with only 1,2 or 3 points according to A-pattern, B-pattern, white lung, respectively.		Early LUS in preterm allows a better assessment of those who are at greater risk of requiring surfactant or MV, before having the oxygenation criteria.		The small sample size and being a **monocentric** study. Patient were lost due to the lack of investigators availability.
Vardar et al.[30]	2020	Turkey	Prospective, cohort	45	mean of 30 (27-32)	Transthoracic	Brat et al score with its 4-grading system* (0,1,2,3).	The LUS score in preterm infants can accurately assess the severity of NRDS.		A cutt-of LUS of 4 predicted the need for a surfactant with 96% sensitivity and 100% specificity. A LUS score of 9 predicted CPAP failure.	The small sample size and the missing follow-up evaluations by determining consecutive doses of surfactant therapy and predicting BPD in preterm infants with NRDS. It is also a **monocentric** study.
Poerio et al.[29]	2020	Italy	Prospective, cohort	100	mean of 37.0 + 5 days Late preterm (13%)	Transthoracic	**Type 1:** hyper echoic appearance - coalescent B lines (white lung) **Type 2:** numerous non-compact B line **Type 3:** normal aerated lung, with the dominance of A lines	LUS performed 30 min after birth, in term and late preterm infants born to CS, has a specificity of 100% and a sensitivity of 71,4% for those who will require NICU admission for NRDS and TTN.			The score used simplifies the description of lung appearance, not acknowledging when the parenchyma is not affected homogeneously. It is also a **monocentric** study.

Szymański et al.[36]	2021	Poland	Prospective, cohort	70	27.3 ± 2.4	Transthoracic	Modified LUS score that substitutes the lateral for the posterior lung field and a 5-grading system** (0,1,2,3,4).		The postnatal (first 24 hours) LUS score has a significant predictive ability for the need for MV on DOL 3.	The diverse spectrum of patients can hinder the standardization of the results, since there might be some not acknowledged confounding factors, also **monocentric** study design.
Raimondi et al.[35]	2021	Italy	Prospective, cohort	240	25-27 (186 ± 6 days) 28-30 (206 ± 6 days) 31-33 (227 ± 6 days)	Transthoracic	Brat et al score with its 4-grading system* (0,1,2,3).		In infants, with GA of 28-30 weeks, the LUS at DOL 7 predicted BPD, with a sensitivity of 78% and specificity of 87%.	The index test used is an imperfect marker of the infant oxygenation status, in hemodynamic instability and poor perfusion.
Jiang et al.[33]	2021	China	Prospective, cohort	88	31.5 ± 4.5	Transthoracic	Modified LUS score with 14 areas (anterior superior and inferior, axillary superior and inferior, posterior superior and inferior, basal lung), with a 6-grading system*** (0,1,2,3,4,5).	A diagnostic threshold of 41.0 points was used to predict the risk of withdrawal failure of MV with a sensitivity of 92,4% and specificity of 93,8%.		The small sample size, the score used only considered the depth of the consolidation and not the intercostal spaces involved. Also, this was a **monocentric** study.
Rodriguez-Fanjul et al.[34]	2022	Spain	Prospective, cohort	40	38 ± 0.6	Transthoracic	Brat et al score with its 4-grading system* (0,1,2,3), scoring > 8.	LUS score can detect dynamic changes in lung aeration, making it a useful tool to assess the optimal PEEP level.		The small sample size, being a **monocentric** study and there wasn't one patient that required MV, which may reflect a lack of "severe" cases, reducing the generalization of this study.

*4-grading system, 0 = A-pattern (defined by the presence of A-lines only or the presence of <3 B-lines); 1 = B-pattern (defined as the presence of ≥3 well-spaced B-lines); 2 = severe B-pattern (defined as the presence of crowded and coalescent B lines, with or without consolidations limited to the subpleural space (alveolar-interstitial syndrome); 3 = extended consolidations; **5-grading system, 0 = normal lung (A-pattern); 1 = B line (B-pattern); 2 = white lung; 3 = white lung and fluid alveologram; 4 = white lung and consolidations; ***6-grading system, 0 = A-pattern, <2 non-fused B-lines; 1 = B1: multiple non-fused B-lines; 2 = B2: dense, partially fused B-lines; 3 = B3: completely fused B-lines; 4 = C1: abnormal pleural line with a small range (depth <1 cm) of subpleural lung consolidation; 5 = C2: abnormal pleural line with extensive (depth >1 cm) lung consolidation; BPD – Bronchopulmonary Dysplasia, CPAP – Continuous Positive Airway Pressure, CS – Cesarian Section, CXR – Chest Radiography, DOL 3 – Day of Life 3, GA – Gestational Age, LUS – Lung Ultrasound, MV – Mechanical Ventilation, RDS – Respiratory Distress Syndrome, TTN – Transient Tachypnea of the Newborn