Lung Ultrasound for the Differential Diagnosis of Respiratory Distress Syndrome and Transient Tachypnea of the Newborn: Systematic Review

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Introduction

Neonatal respiratory distress is one of the most common causes of neonatal intensive care admissions. Intervention and treatment for neonatal respiratory distress vary by disease pathology and progression. Respiratory Distress Syndrome (RDS), occurs in premature infants due to insufficient surfactant production resulting in alveolar collapse[10]. Transient Tachypnea of the Newborn (TTN) occurs due to fluid accumulation (most commonly fetal lung fluid), caused by inadequate expulsion during delivery[4]. Both pathologies present similarly, making it difficult to accurately differentiate between them. Recent evidence has described the utility of lung ultrasound in the critical care setting; however, there are limited reviews comparing lung ultrasound in place of chest Xray (CXR) for the differential diagnosis of TTN and RDS. Given the limitations of CXR, such as low accuracy, ionized radiation exposure and cost, exploring alternative approaches to diagnosis is warranted[2].

For instance, CXR has a sensitivity and specificity of 35% and 85% for the diagnosis of RDS, followed by a sensitivity and specificity of 0% and 98% for TTN[7]. There is emerging evidence outlining the benefits of lung ultrasound in the critical care setting; however, there are limited reviews comparing lung ultrasound in place of CXR for the differential diagnosis of TTN and RDS. Subsequently, there are further limitations to using CXR, such as unnecessary ionized radiation exposure and cost[2]. This review synthesizes studies examining the accuracy of lung ultrasound for the diagnosis of both RDS and TTN, compared to the current gold standard CXR.

P	Newborn infants with symptoms of respiratory distress syndrome (RDS) and/or transient tachypnea of the newborn (TTN)
I	Using lung ultrasound to diagnose and differentiate between RDS and TTN
C	Using chest Xray to diagnose and differentiate between RDS and TTN
O	Measures that define the accuracy of ultrasound in the differential diagnosis of RDS and TTN

Question: In newborns with symptoms of respiratory distress, is lung ultrasound a more effective diagnostic tool to distinguish between TTN and RDS in comparison to bedside CXR?

Search Strategy	
Databases	PubMed, Cochrane Library and Google Scholar
Key Terms	Lung ultrasound, Transient Tachypnea of the Newborn (TTN), Respiratory Distress Syndrome (RDS), Newborn
MeSH Terms	Respiratory Distress Syndrome, Transient Tachypnea of the Newborn, Diagnosis, Differential, Infant, Newborn, Lung ultrasound/diagnostic imaging
Publication Date	<10 Years
Age	24-42 weeks gestation
Article Types	RCTS, Clinical Trials, Systematic Reviews, Meta-Analysis
Critical appraisal conducted using the PEDro scale.	

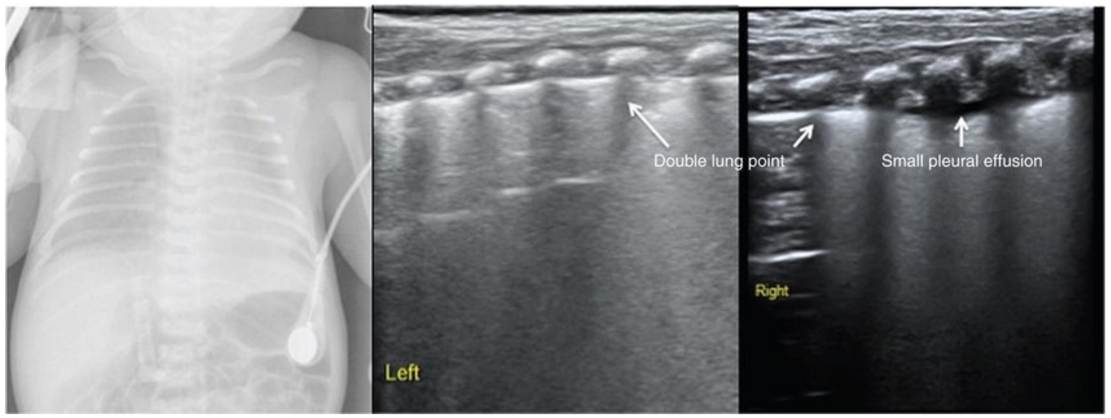

Figure 1. Differentiation between TTN and RDS. Infant was 38 weeks and delivered via cesarian section. Developed progressive dyspnea after birth and was diagnosed with RDS based on clinical and CXR manifestations. However, lung ultrasound showed A line disappearance with no lung consolidation. Confirming TTN as well as the presence of the double lung point, the infant did not require any respiratory interventions 24 hours post delivery consistent with the clinical pathway of TTN[6].

Table 1. Comparison of Included studies

Study	Methodology	Intervention	Outcomes	Limitations
Srinivasan et al., (2022)	Single Center Study	100 pre-term infants admitted to the NICU within six hours of birth. 50 were diagnosed with TTN and 50 were diagnosed with RDS based on clinical presentation, laboratory testing and CXR. Lung ultrasound was performed in each neonate by a senior radiologist blinded to the trial.	100% of neonates in the RDS category concluded lung consolidation with air or fluid bronchograms (p <.001). Presence of Double Lung Point was only evident in TTN group (p <.001).	No randomization of participants. Scored a 7 on the PEDro scale for validity and reliability. Lacks blinding of all subjects.
Gao et al., (2022)	Clinical Practice Report	Lung ultrasound completely replaced CXR in a NICU over a three-year period. 1,381 neonates with respiratory distress were analyzed using lung ultrasound, in place of CXR.	CXR had a 26.3% inaccuracy rate for misdiagnosis and missed diagnosis, whereas lung ultrasound did not have any. Concluded that LUS can safely replace CXR.	No statistical evidence to support practices. Scored a 2 on the PEDro scale, lacked reliability, no blinding was evident, limited comparison group.
Vergine et al. (2014)	Clinical Trial	Neonates with symptoms of respiratory distress received a lung ultrasound within one hour of NICU admission. Images were sent to an external reader blinded to the clinical condition. Final clinical diagnosis was made according to all available data except LUS data. Sensitivity, specificity, PPV, and NPV were calculated comparing lung ultrasound findings to CXR.	LUS showed a sensitivity of 95.6% and specificity of 94.4% with a PPV of 91.6% and NPV of 97.1% for RDS. LUS had a sensitivity of 93.3% and specificity of 96.5% with a PPV of 96.5% and NPV of 93.4% for TTN (p = .001).	Small sample size. Seven neonates included in the final sample size are unaccounted for. Scored a 7 on the PEDro scale, not all subjects were blinded and limited therapeutic blinding.
Liu et al. (2014)	Clinical Trial	Over a period of one year, 60 infants who were diagnosed with TTN were recruited to one study group. Simultaneously, 40 neonates with nonlung disease followed by 20 neonates with RDS were recruited to the control group. Each participant was scanned using lung ultrasound in three regions on both lungs.	Common findings for TTN included a double lung point, interstitial syndromes and pleural line abnormalities (p <.001). Sensitivity and specificity of DLP for diagnosis of TTN was 76.7% and 100%. Common ultrasound findings for RDS neonates was lung consolidation with air bronchograms (p = <.001).	Control and test groups were not equal in comparison. Scored a 7 on the PEDro scale, limited blinding of subjects and no random allocation occurred.

Discussion

The similarities between the clinical presentation of both respiratory distress syndrome (RDS) and transient tachypnea of the newborn (TTN), pose a barrier in the diagnostic approach to treating either pathology. Current practice claims bedside CXR as the gold standard for the diagnosis and differentiation of both pathologies[2]; however, the sensitivity and specificity of CXR for TTN and RDS limits its diagnostic success rates[7]. Moreover, CXR poses its limitations such as unnecessary ionized radiation exposure and specific staffing requirements[2]. This review aimed to highlight the benefit of using Lung ultrasound (LUS) for the diagnosis and differentiation of TTN and RDS. Current research shows that LUS has a higher sensitivity and specificity for diagnosing both RDS and TTN in newborns[11]. Specific clinical manifestations can be determined using LUS including the double lung point in TTN as well as the presence of lung consolidation/air bronchograms in RDS[8]. Both findings show a 100% specificity for their respective pathology, allowing for a concise and accurate diagnosis in comparison to CXR[8]. The benefits of using LUS are not just limited to being a more accurate diagnostic tool, the use of lung ultrasound can also be governed by various clinical professionals such as respiratory therapists, nurse practitioners, sonographers as well as physicians. Greater interprofessional involvement lowers the general cost of diagnostic tools as professionals that are already assigned to the case that requires lung ultrasound intervention can perform the ultrasound themselves[5]. Lastly, LUS has lower rates of misdiagnosis in comparison to bedside CXR, meaning that proper treatment can be implemented early on, limiting disease progression and harm to the neonate[3].

Conclusion

Neonatal lung ultrasound has shown to be effective in the differential diagnosis of respiratory distress syndrome and transient tachypnea of the newborn. Based on this synthesis lung ultrasound appears to have higher accuracy for the diagnosis of TTN and RDS compared with CXR. Future studies that directly compare the accuracies of both approaches in the diagnosis of RDS and TTN are warranted.

Limitations

There are some limitations to this review. One limitation being that there are currently no randomized control trials related directly to the clinical question. Furthermore, some clinical trials included in this review may be susceptible to bias, impacting overall statistical significance.

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