A lung ultrasound-guided strategy for preventing ventilator-associated pneumonia in newborns Clinical Study Protocol

Lead unit: Guangdong Second PeoplesHospital
Project leader:Li Huiyi
Department: Pediatrics
Contact number: 15920384868
Participating units: None
Researchperiod: November1, 202 3to December 31,2025.
Version: V2.0
Version date: October 1, 2023

scenario summary

project name	A lung ultrasound-guided strategy for preventing ventilator-associated pneumonia in newborns
purpose of research	This prospective randomized controlled trial, conducted from December 2023 to December 2025, enrolled full-term newborns requiring continuous mechanical ventilation for over 48 hours. The study evaluated whether a lung ultrasound-guided position adjustment strategy could reduce the risk of ventilator-associated pneumonia (VAP) in these infants compared to the traditional empirical position adjustment protocol.
research design	Eligible infants were randomly assigned in a 1:1 ratio to receive either conventional positioning management or LUS-guided positioning management. The LUS-guided group underwent bedside ultrasound assessments twice daily to monitor for atelectasis or consolidation, with positional adjustments made based on findings to optimize dependent drainage and ventilation-perfusion coupling. Primary endpoints included VAP incidence, while secondary endpoints comprised mechanical ventilation duration, feeding intolerance, pulmonary hemorrhage, pneumothorax, new intracranial hemorrhage, mortality, and ICU length of stay.
Total study cases	94 cases (4 7 cases per group)
Case Selection	Inclusion criteria: Full-term newborns (gestational age 37-42 weeks) requiring continuous mechanical ventilation for over 48 hours. The diagnosis ofVAP follows the guidelines established by the U.S. Centers for Disease Control and Prevention (CDC) (18), applicable to infants under one year old receiving mechanical ventilation for more than 48 hours. Diagnosis requires: chest imaging demonstrating new or progressively worsening pulmonary infiltrates, accompanied by deterioration in gas exchange function.

	Additionally, at least three ofthe following clinical or laboratory findings must be present: abnormal body temperature (rectal temperature>38°C or <35.5°C), leukopenia (WBC <4×109 /L) or leukocytosis (WBC>15×109 /L) with left shift (>10% band cells), purulent or increased tracheal secretions, altered sputum characteristics, increased secretions requiring frequent suction, apnea, signs ofrespiratory distress (tachypnea, chest retractions, wheezing, nasal flaring), abnormal breath sounds , bradycardia (<100 bpm) or tachycardia (>170 bpm).

	Exclusion criteria: ① Premature infants; ② Neonates with early-onset sepsis or prior pneumonia; ③ Patients unsuitable for enteral nutrition; ④ Neonates requiring mechanical ventilation for surgical procedures; ⑤ Infants with multiple congenital anomalies or suspected chromosomal abnormalities. Any ofthese criteria must be met for exclusion from the study.
therapeutic regimen	All infants underwent invasive ventilation via endotracheal intubation using the SLE6000 mechanical ventilator with a heated humidification system, employing disposable respiratory circuits. Both groups received standard NICU care including standardized VAP prophylaxis, antibiotic therapy when indicated, and routine nursing management in accordance with hospital policies and international guidelines. Antibiotic selection and adjustment followed local antimicrobial stewardship guidelines, with modifications based on culture and susceptibility results. The control group received conventional positioning management, while the LUS-guided group utilized lung ultrasound-guided positioning management.

Efficacy Evaluation	Effectiveness evaluation indicators (main efficacy indicators and secondary efficacy indicators) Main therapeutic index: the effect of lung ultrasound-guided positioning management on the incidence of ventilator-associated pneumonia in newborns with mechanical ventilation. Secondary efficacy endpoints included feeding intolerance in newborns, pulmonary hemorrhage, pneumothorax, new-onset intracranial hemorrhage, mortality, duration of invasive mechanical ventilation (from initiation to successful extubation or death), and NICU length of stay.
	Safety evaluation indicators: mortality and complication incidence

Statistical Methods	Statistical analysis was performed using IBM SPSS Statistics (version 20.0; IBM Corporation, Amherst, New York, USA). Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) based on their distribution patterns, while categorical data were expressed as frequencies and percentages. Categorical variables were compared using chi-square test or Fishers exact test, whereas continuous variables were analyzed using independent samples t-test or Mann-Whitney U test as appropriate. A two-tailed P-value <0.05 was considered statistically significant. This analysis strictly followed the original research protocol, with all procedures conducted as planned.
Study duration	From November 1, 202 3to December 31,2025

I. Research Background

Ventilator-associated pneumonia (VAP) ranks among the most prevalent and severe nosocomial infections in neonatal intensive care units (NICU), leading to prolonged mechanical ventilation, extended hospital stays, and increased mortality. The incidence of neonatal VAP (Neo-VAP) varies significantly across different monitoring criteria and patient populations: in high-income countries, it ranges from 1.4 to 7 cases per 1,000 ventilator days, while in developing countries, the figure can reach up to 89 cases per 1,000 ventilator days. [1,2] 。

Premature infants and extremely low birth weight infants are exposed to invasive ventilation due to immature immune defense, impaired mucosal ciliary clearance function, and prolonged exposure to invasive ventilation [3,4] , which is high risk.

The pathogenesis of novel VAP involves three key mechanisms: microaspiration of contaminated secretions, colonization of biofilm on tracheal intubation, and gravity-dependent accumulation of airway secretions. [5] Inappropriate or static postures may exacerbate lung collapse and secretions retention, leading to ventilation-perfusion mismatch, hypoxemia, and bacterial overgrowth. Studies in adult and pediatric patients demonstrate that appropriate positioning interventions—such as semi-recumbent or prone positions—can improve oxygenation and potentially reduce VAP incidence. [6,7] However, these strategies have not been sufficiently standardized or validated in newborns, as their immature thermoregulation and unstable hemodynamics limit frequent positional adjustments. [8-10] 。

Lung ultrasound (LUS) has emerged as a reliable, radiation-free bedside imaging tool for dynamic assessment of pulmonary ventilation, atelectasis, and consolidation in newborns. [11-13] The quantitative LUS score provides real-time assessment of regional ventilation, enabling early detection of asymmetric ventilation patterns. [14,15] By incorporating LUS findings into positional management, we can develop physiologically based strategies to optimize lung re-expansion and secretions clearance before irreversible infection occurs.

However, clinical evidence supporting this approach in newborns remains limited. To address this, our study evaluated the clinical effectiveness of lung ultrasound-guided targeted interventions in preventing mechanical ventilation-associated pneumonia (Neo -VAP). We hypothesized that LUS-guided personalized interventions would reduce VAP incidence and improve respiratory function compared to conventional care-guided positioning.

II. Research Objectives

1. The primary objective was to evaluate whether a lung ultrasound-guided positioning strategy could reduce the risk of ventilator-associated pneumonia (VAP) in mechanically ventilated newborns compared to traditional empirical positioning protocols.

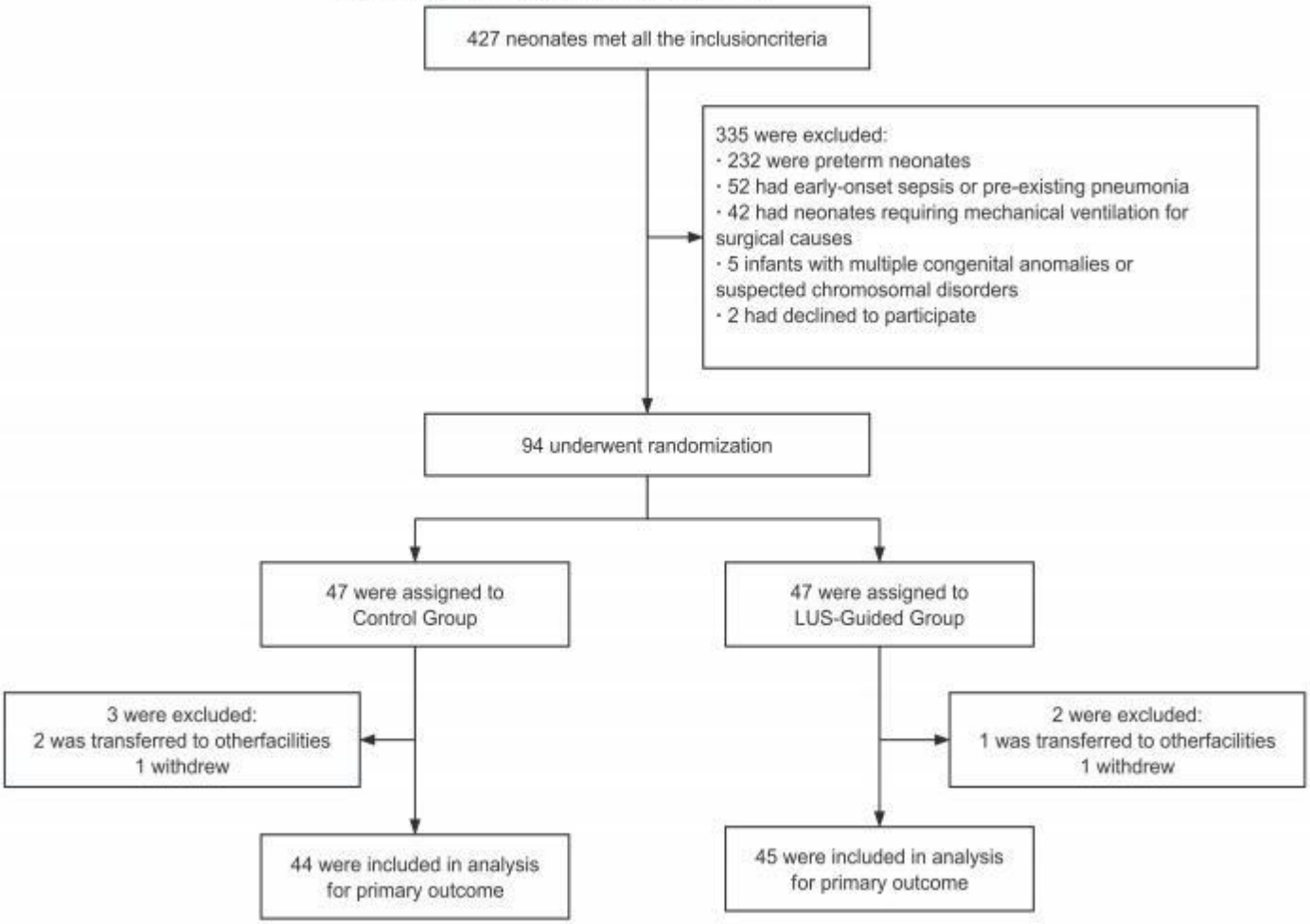
2. Secondary objective: To enhance the effectiveness ofVAP prevention in newborns and expand the clinical applications of ultrasound technology.

III. Types of research design, principles and experimental steps

1. research design

This prospective randomized controlled trial was conducted from December 2023 to December 2025 atthe Tertiary ICU ofGuangdong Second Peoples Hospital, enrolling full-term newborns requiring continuous mechanical ventilation for over 48 hours. Eligible infants were randomly assigned in a 1:1 ratio to receive either conventional position management or LUS-guidedposition management. The LUS-guided group underwent bedside ultrasound assessments twice daily to monitor atelectasis or consolidation, with position adjustments made based on evaluation results to optimize dependent drainage and ventilation-perfusion matching. Primary outcome was VAP incidence, while secondary outcomes included mechanical ventilation duration, feeding intolerance, pulmonary hemorrhage, pneumothorax, new intracranial hemorrhage, mortality, and ICU length of stay.

2.stages of research



IV. Case Selection

This prospective randomized controlled trial was conducted from December 2023 to December 2025 at the tertiary ICU of Guangdong Second Peoples Hospital, enrolling full-term newborns requiring continuous mechanical ventilation for over 48 hours.

1. Selection criteria

All enrolled newborns underwent prospective observation to monitor the incidence of ventilator-associated pneumonia (VAP). VAP diagnosis was based on the criteria established by the U.S. Centers for Disease Control and Prevention (CDC). [16] This is indicated for infants under one year of age receiving mechanical ventilation for more than 48 hours. Diagnosis requires: chest imaging demonstrating new or progressive pulmonary infiltrates with deterioration of gas exchange function.

Additionally, at least three of the following clinical or laboratory findings must be present: abnormal body temperature (rectal temperature>38°C or <35.5°C), leukopenia (WBC <4×10⁹ /L) or leukocytosis (WBC>15×10⁹ /L) with left shift (>10% band cells), purulent or increased tracheal secretions, altered sputum characteristics, increased secretions requiring frequent suction, apnea, signs of respiratory distress (tachypnea, chest retractions, wheezing, nasal flaring), abnormal breath sounds (rheumus, crackles, or snoring), bradycardia (<100 bpm) or tachycardia (>170 bpm).

2. Exclusion criteria

① premature；

② Neonates with early sepsis or previous pneumonia;

③ Not suitable for patients with enteral nutrition;

④ Newborns requiring mechanical ventilation due to surgery;

⑤ There are many infants with congenital abnormalities or suspected chromosomal abnormalities.

Those who meet any ofthe above criteria will be excluded and excluded from this study.

3. Filter criteria

Participants enrolled in the group who meet one of the following criteria should be excluded:

(1) Those who do not meet the inclusion criteria or meet the exclusion criteria after inclusion.

(2)No record.

(3) Individuals who have not used the trial drug or intervention.

The analysis set is determined by a blind review meeting to exclude cases. The reasons for exclusion should be documented, and the original data should be retained for reference.

4.Drop/Exit criteria

Drop/Exit criteria:

(1) The chiefphysician considers that the clinical condition is not suitable for further experimentation;

(2) If there is a discrepancy between clinical symptoms and other auxiliary examinations and the results ofrelevant non-invasive examinations;

(3) Parents who do not agree to continue the experiment during the experiment

5. Termination criteria

(1) If the following complications occur during the experiment: cardiac arrest, intestinal perforation, intracranial complications, etc.;

(2) Those who need to be rescued and are not suitable for experimental operations;

(3) The chiefphysician considers that the clinical condition is not suitable for further experimentation;

(4) If there is a discrepancy between clinical symptoms and other auxiliary examinations and the results ofrelevant non-invasive examinations;

(5) Parents who refuse to continue the experiment during the experiment

V. Research Methods and Technical Routes

This prospective randomized controlled trial was conducted from December 2023 to December 2025 at the Tertiary ICU of Guangdong Second Peoples Hospital, enrolling full-term newborns requiring continuous mechanical ventilation for over 48 hours. Eligible infants were randomly assigned in a 1:1 ratio to receive either conventional position management or LUS-guided position management. The LUS-guided group underwent bedside ultrasound assessments twice daily to monitor atelectasis or consolidation, with position adjustments made based on evaluation results to optimize dependent drainage and ventilation-perfusion matching. Primary outcome was VAP incidence, while secondary outcomes included mechanical ventilation duration, feeding intolerance, pulmonary hemorrhage, pneumothorax, new intracranial hemorrhage, mortality, and ICU length of stay.

VI. Observation items and testing time points

All infants underwent invasive ventilation using the SLE6000 mechanical ventilator with a heated humidifier via endotracheal intubation, employing disposable respiratory circuits. Both groups received standard NICU care, including standardized VAP prophylaxis, antibiotic therapy when indicated, and routine nursing management in accordance with hospital protocols and international guidelines. Antibiotic selection and adjustment followed local antimicrobial stewardship guidelines, with modifications based on culture and susceptibility test results.On the 1st, 3rd and 7th day of mechanical ventilation, chest radiographs were taken in the positive and lateral positions respectively, and repeated examinations were made according to clinical needs.

Control group (standard positioning management)

Infants in the control group had their positions adjusted every two hours, alternating between supine, left lateral, right lateral, and prone positions. [17] The head of the bed should be elevated 15°-30° with the body in a slightly flexed position—hips aligned along the midline, shoulders slightly forward, head centered, and arms

free to move. Position adjustments should only be made when vital signs are stable and resuscitation is delayed, or when adjusting the ventilator, administering IV fluids, or managing deep sleep. If heart rate fluctuates more than 20 beats per minute or SpO2 drops below 90% (excluding airway obstruction), the interval between position adjustments should be extended to 3-4 hours. This group did not undergo ultrasound evaluation.

LUS Guided Group (Lung Ultrasound Guided Localization)

Postural adjustments follow three principles: ensuring effective drainage of the affected lung area, optimizing ventilation of the healthy area, and preventing stress-related injury [16,18] In addition to routine care, two LUS assessments are conducted at fixed times daily (08:00 and 18:00) to guide individualized position adjustments by monitoring regional ventilation.

• If unilateral atelectasis or pulmonary edema is detected, the patient should first be maintained in dependent lateral position for approximately 1 hour, then transition to the contralateral or prone position for 3 hours.

• For lesions previously managed by the department, the prone position duration is reduced to 1 hour, while supine or lateral positions are extended to 3 hours.

• For posterior lesions, the supine or lateral position should be limited to 1 hour, while the prone position should be extended to 3 hours.

• Resume the standard two-hour shift system once the symptoms or edema have subsided.

If SpO2 remains persistently below 90% (excluding operational or feeding disturbances), the respiratory rate increases by more than 20 breaths per minute from baseline, or airway secretions significantly increase, an additional LUS evaluation is required.

All ultrasound examinations are performed by two pediatricians with professional training, while the imaging data undergoes quality review by senior neonatologists with pulmonary ultrasound experience. All physicians receive semi-annual intensive care ultrasound hands-on training from internationally certified instructors to ensure consistent diagnostic standards and standardized technical procedures.

VII. Criteria for efficacy evaluation

Main efficacy criteria: the effect of lung ultrasound-guided positioning management on the incidence of ventilator-associated pneumonia in mechanical ventilation newborns.

Secondary efficacy criteria included feeding intolerance in newborns, pulmonary hemorrhage, pneumothorax, new intracranial hemorrhage, mortality, duration of invasive mechanical ventilation (from initiation to successful extubation or death), and NICU hospitalization duration.

VIII. OBSERVATION OF ADVERSE EVENTS

Adverse event monitoring: During the trial, clinicians should continuously monitor the childs vital signs. If clinical symptoms or auxiliary findings (e.g., heart rate, liver size, mental status, X-ray, blood gas analysis) contradict non-invasive test results, the trial should be immediately terminated and the attending physician should be promptly consulted.

IX. Data security monitoring

Clinical trials will establish data safety monitoring plans based on risk levels. All adverse events will be meticulously documented, properly managed, and tracked until resolved or stabilized. Serious adverse events and unexpected incidents must be promptly reported to ethics committees, regulatory authorities, sponsors, and drug regulatory agencies as required. Principal investigators will conduct periodic cumulative reviews of all adverse events, and when necessary, convene investigator meetings to evaluate the risks and benefits of the trial. For double-blind trials, emergency unblinding may be conducted when required to ensure participant safety and rights. Studies exceeding the minimum risk threshold will have independent data monitors assigned to oversee data collection. High-risk studies will establish independent data safety monitoring committees to review cumulative safety and efficacy data, providing recommendations on whether to continue the trial.

X. Statistical processing

Statistical analysis was performed using IBM SPSS Statistics (version 20.0; IBM, Inc., Amherst, New York, USA). Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) based on their distribution patterns, while categorical data were expressed as frequencies and percentages. Categorical variables were compared using chi-square test or Fishers exact test, whereas continuous variables were analyzed using independent samples t-test or Mann-Whitney U test as appropriate. A two-tailed P-value <0.05 was considered statistically significant. All procedures were conducted strictly in accordance with the original research protocol.

XI. ETHEICAL ASPECTS OF CLINICAL RESEARCH

Clinical research will adhere to the World Medical Conferences Helsinki Declaration and related regulations. The study will only commence after obtaining approval from the ethics committee for the trial protocol. Before enrolling any participant, researchers must provide a complete and comprehensive explanation of the studys objectives, procedures, and potential risks to the participant or their representative, who must sign a written informed consent form. Participants should be informed of their right to withdraw from the study at any time, and the informed consent document must be retained as part of the clinical research records for review. Throughout the study, participants personal privacy and data confidentiality will be strictly protected.

XII. STUDY PROGRESS

time	research contents
April 2024-December 2024	Trial preparation phase ① Prepare relevant instruments and equipment, as well as equipment maintenance, testing, and parameter calibration; ② Staff recruitment and training, clear division of labor and work content, familiar with the test process; ③ Complete the pre-experiment.
January2025-December 2025	Recruit subjects and conduct clinical trials ① Recruit research subjects and implement interventions according to the randomized protocol; ② Record test data.
January2026-March 2026	Write scientific research papers and project summary reports ① Organize and analyze research data; ② Scientific research paper writing and submission; ③ Summarize research results and write project summary report.

XIII. Participants

surname and personal name	Title/Field of Study	divide the work	Ethics training course name and time

Li Huiyi	Associate Head Nurse/Nursing	project leader	2021-07-09
Hudaiju	Intermediate/Nursing	conceptual design	
Liang Zhenyu	Senior Associate Pediatrician	conceptual design	2021-07-10
Huang Xihua	Associate Head Nurse/Nursing	Specific experiments and data collection	2021-07-09
Meng Qiong	Senior Physician/Pediatrics	DA	2021-07-09
Yang Qiaohuan	Senior Associate Pediatrician	Data analysis and quality control	2021-07-13
Chen Na	Intermediate/Pediatric	Specific experiments and data collection	2021-07-13
Li Lin	Primary/Pediatric	Specific experiments and data collection	

XIV. References

［1］1.Rangelova S, Madzharova K, Dimitrova M. Ventilator-associated pneumonia in the neonatal intensive care unit: epidemiology, prevention and diagnosis. Diagnostics (Basel). 2024;14(5):505. [PMCID: PMC10854825]

［2］Rosenthal VD et al. International Nosocomial Infection Control Consortium (INICC) report, 2012–2020: device-associated infection rates from neonatal intensive care units worldwide. Am J Infect Control. 2021;49(12):1424-1433. doi:10.1016/j.ajic.2021.05.021

［3］Thatrimontrichai A et al. Ventilator-associated pneumonia in neonates: a prospective observational study. J Perinatol. 2017;37(6):669-674. doi:10.1038/jp.2017.11

［4］Dang J et al. Risk factors and outcomes of ventilator-associated pneumonia in a neonatal intensive care unit: a retrospective cohort study. BMC Infect Dis. 2023;23(1):115. doi:10.1186/s12879-023-08073-x

［5］Howroyd C et al. Ventilator-associated pneumonia: pathobiological heterogeneity and diagnostic challenges. Nat Commun. 2024;15:1548. doi:10.1038/s41467-024-50805-z

［6］Oczkowski S et al. Body position for preventing ventilator-associated pneumonia in adults: systematic review and network meta-analysis. Cochrane Database Syst Rev. 2022;3:CD009946. PMCID: PMC8864849

［7］7.Pawlik AJ et al. Ventilator-associated pneumonia prevention in pediatric patients: review of evidence-based practices. Front Pediatr. 2023;11:960067. PMCID: PMC9600673

［8］Rivas-Fernandez M et al. Infant position in neonates receiving mechanical ventilation. Cochrane Database Syst Rev. 2016;11:CD003668. PMID: 27819747

［9］Hough JL et al. Effect oftime and body position on ventilation in premature infants. Pediatr Res. 2016;80(4):499-504. doi:10.1038/pr.2016.116

［10］.Loi B et al. Respiratory and haemodynamic effects of six-hour pronation in ventilated neonates: a prospective observational study. EClinicalMedicine. 2023;58:101904. doi:10.1016/j.eclinm.2023.101904

[11] Corsini I et al. Lung ultrasound in neonatal critical care: evidence and perspectives. Pediatr Pulmonol. 2020;55(9):2504-2518. doi:10.1002/ppul.24960

[12] Ruoss JL et al. Lung ultrasound in the neonatal intensive care unit. Children (Basel). 2021;8(12):1098. doi:10.3390/children8121098

[13] YousefN et al. Lung ultrasound monitoring in neonatal and pediatric intensive care. Eur J Pediatr. 2023;182(1):43-55. doi:10.1007/s00431-022-04750-0

[14] Raimondi F et al. Neonatal lung ultrasound score and postnatal adaptation in term and preterm infants. Pediatrics. 2021;148(3):e2021051467. doi:10.1542/peds.2021-051467

[15] Szymański P et al. Modified lung ultrasound score predicts ventilation requirements in neonatal respiratory distress syndrome. BMC Pediatr. 2021;21(1):17. doi:10.1186/s12887-020-02485-z

[16] Klompas M, Branson R, Eichenwald EC, et al. Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 update. *Infect Control Hosp Epidemiol.* 2022;43(6):687–713. doi:10.1017/ice.2022.74.

[17] Gupta S, Suryawanshi P, Kadam M, et al. Incidence and outcomes of ventilator-associated pneumonia in a neonatal intensive care unit. *J Trop Pediatr.* 2020;66(6):596–603. doi:10.1093/tropej/fmaa050.

[18] Centers for Disease Control and Prevention (CDC). *NHSN Ventilator-Associated Event (VAE) and Pneumonia (PNEU) Protocols, 2025 Edition.*