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RESEARCH ARTICLE

Use of lung ultrasound to guide surfactant administration and make differential diagnosis during immediate and transitional newborn care in a perinatal hospital

Daniel Ibarra-Ríos[1,2], Federico Franchi[3], Deneb A. Morales-Barquet[4], Edgar A. Jorge-Chang[4], Carolina Valencia-Contreras[4], Juvenal Salgado-Valencia[4], Irma A. Coronado-Zarco[4], Alejandra Sánchez-Cruz[5], and Horacio Márquez-González[2]*

[1]Expresidente, Asociación de Neonatólogos de la Ciudad y Valle de México, Ciudad de México; [2]Servicio de Investigación Clínica, Hospital Infantil de México Federico Gómez, Ciudad de México. México; [3]Departamento de Neonatología, Azienda Ospedaliera Carlo Poma, Mantova, Italia; [4]Departamento de Neonatología, Instituto Nacional de Perinatología Isidro Espinosa de los Reyes, Ciudad de México; [5]Departamento de Neonatología, Unidad Médica de Alta Especialidad, Hospital de Gineco Obstetricia No. 4, Luis Castelazo Ayala, Ciudad de México. México

Abstract

Introduction: *Lung ultrasound (LU) has proven to be the best method for diagnosing surfactant deficiency (Respiratory Distress Syndrome [RDS]) and continuous positive airway pressure (CPAP) failure; experience in Mexico is limited.* **Methods:** *The objective was to determine the usefulness of a LU program and a lung ultrasound score (LUS) for predicting surfactant need in a perinatal hospital. LUS and FiO_2 of patients who received or did not receive surfactant were compared with Mann-Whitney U test. Using LU as the gold standard, FiO_2 thresholds were tested using receiver operating characteristic curves.* **Results:** *69 newborns (33 weeks [30, 35]; birth weight 1925 [1470, 2590]) were evaluated for differential diagnosis and to determine surfactant needs. 74 studies were performed: 54 for the first dose (14 administrations, 26%) and 20 for re-surfactant (six administrations, 30%). Among the group evaluated for a first dose, LU diagnoses were RDS 30%, transient tachypnea of the newborn (TTRN) 59%, TTN/air leak 6%, TTRN/pleural effusion 1.6%, congenital pneumonia 1.6%, and meconium aspiration syndrome 1.6%. There was a statistically significant difference between the LUS of patients who received the first (12 [10, 12] vs. 6 [5, 6]) and second dose of surfactant (12 [11, 12] vs. 4 [4, 7]). $FiO_2 \geq 30\%$ was found in 34% of patients with TTN pattern in whom CPAP optimization improved all cases. An optimal FiO_2 threshold of 24% was found with an area under the curve of 0.85.* **Conclusions:** *LU provides very valuable information through pattern recognition and a LUS, allowing differential diagnosis and tailored physiological care.*

Keywords: *Lung ultrasound. Neonatology. Ultrasound. Respiratory distress syndrome. Transient tachypnea of the newborn. Surfactant. Neonatology. Continuous airway pressure.*

Uso del ultrasonido pulmonar para guiar la administración de surfactante y realizar diagnóstico diferencial durante la atención neonatal inmediata y de transición en un hospital perinatal

Resumen

Background: *El ultrasonido pulmonar (UP) es el mejor método para diagnosticar deficiencia de surfactante (SDR) y la falla de la presión positiva continua de la vía aérea (CPAP); la experiencia en México es limitada.* **Métodos:** *El objetivo fue deter-*

***Correspondence:**
Daniel Ibarra-Ríos
E-mail: ibarraneonato@gmail.com

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minar la utilidad de un programa de UP y una escala semicuantitativa (ESC) para predecir la necesidad de surfactante en un hospital perinatal. La ESC y la FiO_2 de los pacientes que recibieron o no surfactante se compararon mediante la prueba U de Mann-Whitney. Utilizando el UP como estándar de oro, se evaluaron los umbrales de FiO_2 mediante curvas ROC. **Resultados:** *Se evaluaron 69 recién nacidos (33 semanas [30-35]; peso al nacer 1.925 [1.470-2.590]) para diagnóstico diferencial y determinar la necesidad de surfactante. Se realizaron 74 estudios: 54 para primera dosis (14 administraciones, 26%) y 20 para resurfactar (seis administraciones, 30%). Entre el grupo evaluado para una primera dosis, los diagnósticos por UP fueron SDR 30, taquipnea transitoria del recién nacido (TTRN) 59%, TTRN/fuga aérea 6%, TTRN/derrame pleural 1.6%, neumonía congénita 1.6% y SAM 1.6%. Hubo una diferencia estadísticamente significativa entre la ESC de los pacientes que recibieron la primera (12 [10-12] vs. 6 [5-6]) y segunda dosis de surfactante (12 [11-12] vs. 4 [4-7]). Se encontró una FiO_2 ≥ 30% en el 34% de los pacientes con TTN, a quienes el optimizar la CPAP mejoró todos los casos. Se encontró un umbral óptimo de FiO_2 del 24% con un área bajo la curva de 0.85.* **Conclusiones:** *El UP proporciona información muy valiosa mediante el reconocimiento de patrones y una ESC, lo que permite el diagnóstico diferencial y la atención fisiológica personalizada.*

Palabras clave: *Ultrasonido pulmonar. Síndrome de dificultad respiratoria. Taquipnea transitoria del recién nacido. Surfactante. Neonatología. Presión continua de la vía aérea.*

Introduction

Initial stabilization in the delivery room is guided by international neonatal resuscitation guidelines, maintaining adequate ventilation and airway patency, offering respiratory support during transition, and avoiding maneuvers that may cause lung damage.

Current management in preterm infants with spontaneous breathing is the use of non-invasive ventilation as initial respiratory support, preferring nasal continuous positive airway pressure (CPAP) as the first option from the delivery room, due to its accessibility, as well as safety and efficacy. In patients routinely managed with CPAP before surfactant administration, a decrease in the risk of bronchopulmonary dysplasia (BPD) or death has been demonstrated, so it is considered a standard of practice[1-5]. Currently, surfactant is administered in newborns requiring FiO_2 > 30%, based on CPAP failure studies[6,7]. More recent studies have shown that FiO_2 > 30% at 2 h of life fails to identify up to 50% of infants who were finally given surfactant, and optimal prediction thresholds have been described as low as 23%[8,9].

Less invasive surfactant administration (LISA) has become the preferred method of surfactant delivery. This technique has been shown to decrease the composite outcome of death or BPD, the need for ventilation, and the presence of BPD among survivors[10].

Lung ultrasound (LU) has proven to be the best method to diagnose surfactant deficiency (Respiratory Distress Syndrome [RDS]) and predict CPAP failure[11,12]. Its use has shown an increase in the proportion of neonates receiving surfactant within the first 3 h with a lower maximum FiO_2 before treatment; also, a lower pCO_2, a decrease in the duration of invasive ventilation, and an increase in the number of ventilator-free days have been demonstrated[13,14]. Epoch studies have proven that there is no increase in the use of surfactant due to the introduction of LU to decide its administration[15]. Although programs have been established since 2018, the experience in Mexico is limited.

Methods

The objective of this study was to determine the usefulness of a LU program and the lung ultrasound score (LUS) to determine the need for surfactant and make differential diagnosis in a perinatal hospital during immediate care (delivery room and transitional nursery).

Approval from the ethics committee was obtained for the analysis of routinely obtained and anonymized clinical data, so informed consent was waived. The study was performed in a tertiary-level care perinatal hospital. Routine practice included delayed cord clamping, early CPAP administration with a T-piece during neonatal resuscitation with immediate transition to CPAP in the delivery room, early caffeine, and early rescue surfactant treatment within the first 3 h. Surfactant administration was performed with the LISA technique if the patient was not intubated.

From October 1st, 2023, to September 30, 2024, a point-of-care ultrasound service was available. Consults were made at the discretion of the attending neonatal team secondary to RDS suspicion, FiO_2 ≥ 30% or doubt in interpreting chest radiography (CXR). The consultation consisted of a full LU with the calculation of a LUS with the Brat scoring system neonatal adaptation[16].

LU was performed with the available equipment in the delivery room. Equipment used during the study was as follows:

- Acuson x300® (Siemens Healthcare, Munich, Germany) with a 5-14 Mz linear transducer (hockey stick)
- Logiq E® (GE Healthcare, Chicago, Illinois, USA) with a 9-12 Mz linear transducer
- Handheld CHISON SonoEye P1® (Medical Technologies Co., LTD, Jiangsu, China) with a 9-14 Mz linear transducer.

Six regions of the anterior and lateral thorax were explored with 6-10 s clips from medial to lateral longitudinal scans (anterior, inferior, and lateral; right and left) recorded. DIR, FF, EAJC, and DAMB performed studies. DIR was responsible for overviewing, reporting, and decision-making regarding LU consults.

For the first time, consults LUS was calculated with a minimum of 1 h (1-2 h) of life through both transverse and longitudinal scans, with the following scores:

- 0, defined by the presence of A-lines and pleural sliding
- 1, defined as the presence of three or more well-spaced B-lines
- 2, defined as the presence of coalescent B-lines giving a white lung appearance also known as the ground glass sign
- 3, defined as the presence of extended consolidations, also known as the snowflake sign.

The RDS pattern was defined as a homogeneous loss of lung aeration with diffuse alveolar pattern (white lung); without normal zones; thickened, irregular pleural line with consolidations and small pleural effusion could also be found. LUS at the diagnosis ≥ 9[17].

Transient tachypnea of the newborn (TTN) pattern was identified by a heterogeneous interstitial pattern alternating with at least one normal zone (A-pattern); absence of consolidations; relatively regular and non-thickened pleural line. LUS at the diagnosis ≤ 7.

Pneumothorax was diagnosed with the absence of pleural sliding and any parenchymal sign (A-lines with any B-line), absence of lung pulse, and the barcode sign on M-Mode. Pneumomediastinum was diagnosed by the absence of lung sliding on limited parasternal scan, presence of a "still" lung point (pleural sliding present in both lungs along the mid-clavicular zones but absent in the parasternal areas), and thick linear/curvilinear echogenic lines, within the margins or in the thymic parenchyma (air)[18].

Neonatal pneumonia was diagnosed with the shred sign, persistent consolidation with air bronchogram alternating with areas with alveolar interstitial syndrome integrated with a clinical construct indicating infection.

Meconium aspiration syndrome (MAS) features were a bilateral diffuse and irregular alveolar interstitial pattern and evolving atelectasis due to meconium plugging. Consolidations with bronchograms and pleural effusion could also be found.

LUS and FiO_2 of patients who received or did not receive surfactant were compared with the Mann-Whitney U test. Using LU as the gold standard, FiO_2 thresholds were tested using receiver operating characteristic (ROC) curves. Statistical analysis was performed using SPSS 23.0 (IBM).

Results

From October 1st, 2023, to September 30, 2024, a total of 505 consultations were conducted. Seventy-four of them (15%) were conducted in immediate newborn care (54 to assess the need for the first dose of surfactant and make a differential diagnosis, and 20 to assess the need for a second surfactant dose) in 69 infants (33 weeks [30, 35] and birth weight 1925 [1470, 2590]). 88% had maternal pathology, 88% had cesarean sections, 54% received positive pressure ventilation, and 17% were intubated during resuscitation (30% were intubated at some point during intensive/intermediate care) (Table 1). Patients were studied under mechanical ventilation 20%, CPAP 72%, nasal ventilation 3%, and indirect oxygen 5%.

Within the group evaluated for the first time, LU diagnoses were RDS 30%, TTN 59%, TTN and pneumothorax 4%, TTN and pneumomediastinum 1.6%, TTRN and pleural effusion 1.6%, congenital pneumonia 1.6%, and MAS 1.6% (Fig. 1).

Surfactant was indicated in 15 of 54 first-time consults (28%). The procedure was made with LISA in 11 patients (79%) and by the endotracheal tube in 3 patients (21%), one of them with massive meconium aspiration. The two patients with borderline RDS pattern improved after CPAP adjustment and did not required surfactant.

The second dose of surfactant was indicated in 6 of 20 consults (30%). Five by the endotracheal tube (83%) and one as a second LISA procedure.

There was a statistically significant difference between LUS and FiO_2 in patients who received the first (LUS/FiO_2 12 [10, 12]/35 [30, 40] vs. 6 [5, 6]/25 [21, 30]) and second dose of surfactant (12 [11, 12]/37 [28/49] vs. 4 [4, 7]/26 [25, 28]) (Fig. 2).

Table 1. Demographic characteristics

Demographic	Median (interquartile range), n (%)
In hospital prenatal care	45 (65)
Adequate prenatal care	58 (84)
Prenatal steroids	17 (24)
Magnesium Sulfate	21 (30)
Maternal age	29 (24, 35)
Gravida	2 (2, 3)
Maternal pathology	61 (88)
Chorioamnionitis	6 (9)
Early onset sepsis	16 (23)
Healthcare-associated infection	22 (32)
Premature rupture of membranes	18 (26)
Gestational age	33 (30, 35)
Birth weight	1925 (1470, 2590)
Intrauterine growth restriction	16 (23)
Cesarean section	61 (88)
Positive Pressure Ventilation	37 (54)
Intubation during resuscitation	12 (17)
Intubated during hospital stay	21 (30)
Apgar 1	8 (7, 8)
Apgar 5	9 (8, 9)
Asphyxia	1 (1.5)
Necrotizing enterocolitis	12 (17)
Intraventricular hemorrhage	11 (16)
Retinopathy of prematurity	5 (7)
Bronchopulmonary dysplasia	24 (34)
Mortality	5 (7)

FiO_2 ≥ 30% was found in 34% of patients with TTN pattern than in whom CPAP optimization and pronation were recommended, showing improvement in all cases.

In the 14 patients evaluated with surfactant-modified RDS who did not require a second dose, one pneumothorax, one pneumomediastinum, and one pneumonia were found. Antibiotic management was recommended in two patients (2.8%).

Considering LU as the gold standard, ROC curves for predicting the need for surfactant found an optimal FiO_2 threshold of 24% with an area under the curve (AUC) of 0.85 (Fig. 3).

Five patients died, two with extreme prematurity and related complications, one with Down syndrome, one with massive meconium aspiration and asphyxia, and one with a complex dysmorphic syndrome.

Discussion

For its availability, an FiO_2 ≥ 30% has been used to identify CPAP failure and decide surfactant administration. Other clinical parameters used are $SatO_2/FiO_2$ ratio ≤ 348 and LUS ≥ 9. An integrated multivariate model including all the former showed a high predictive accuracy with an AUC of 0.95; nevertheless, LUS ≥ 9 demonstrated the highest sensitivity (91%) and specificity (81%) as an individual predictor [19].

CPAP from the delivery room onward as an alternative to routine intubation is considered standard of care. CPAP mechanically splints the upper airway, distends the lower airway, reduces resistance to air flow, and therefore diminishes ventilation-perfusion mismatch, improving oxygenation; by preventing alveolar collapse, it reduces protein leaks and helps maintain surfactant. In our study, two patients with an RDS pattern with borderline LUS improved after CPAP adjustment without the need for exogenous surfactant. Dargaville and collaborators demonstrated that at more mature gestation's surfactant deficiency might be less pronounced and can be sustained by CPAP alone[20].

LUS showed its usefulness to decide a second dose of surfactant when there was clinical doubt with a clear statistical difference (12 [11, 12] vs. 4 [4, 7]). Several studies have been conducted to identify predictors of LISA failure. A recent study found that the best predictors were gestational age, intrauterine growth restriction, temperature at admission, $SatO_2/FiO_2$ ratio, and LUS. The model showed an AUC 0.84 (95% CI, 0.75-0.93, $p < 0.001$). LUS ≥ 12 in a study performed 60-120 min after the LISA procedure increases the possibility of CPAP failure by 6.4 times and was the most impactful factor in the model[21].

A term proposed by Mary Ellen Avery since 1966[22], TTN affects approximately 7-10% of all newborns[23]. Initially coined to describe a condition where other causes of respiratory distress were excluded. A better understanding of the pathophysiology and biology of TTN has recently been clarified[24]. The alveolar space is directly proportional to gestational age, while the density of lung tissue is inversely proportional; although

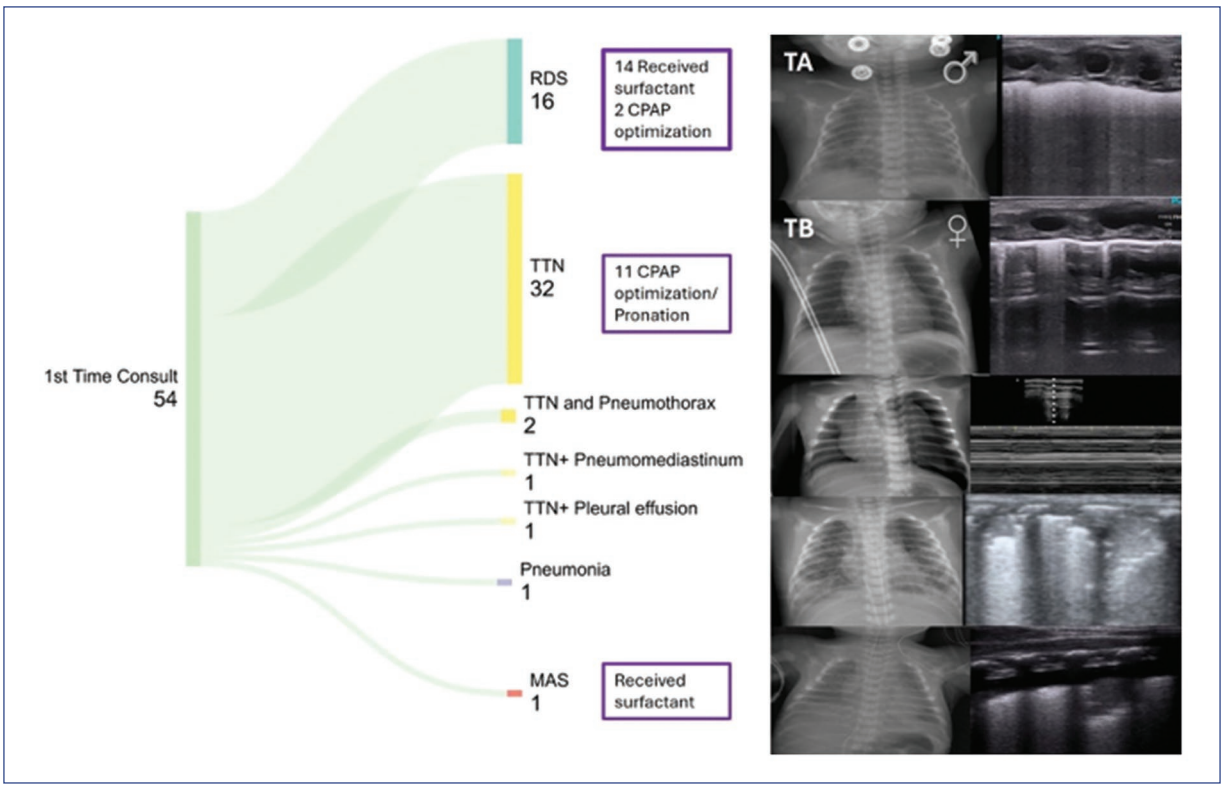

Figure 1. LU assessment to determine the need for surfactant and make differential diagnosis. Examples of CXR and LU are shown. A case of 34 weeks of gestation twins. Twin A developed RDS, at the time of consult CPAP of 6 and FiO_2 of 45% with pre ductal saturation of 94% ($SatO_2/FiO_2$ = 209) receiving surfactant with LISA technique. Twin B showed a TTN pattern, at the time of consult CPAP of 6 and FiO_2 of 25% with pre ductal saturation of 92% ($SatO_2/FiO_2$ = 368). RDS: respiratory distress syndrome; TTN: transient tachypnea of the newborn; MAS: meconium aspiration syndrome; LU: lung ultrasound; CPAP: continuous positive airway pressure; CXR: chest radiography.

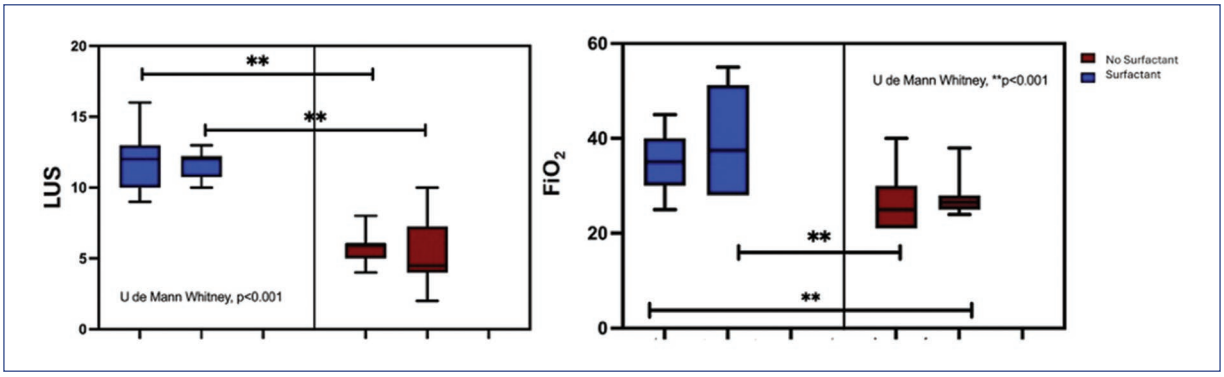

Figure 2. Rank difference between lung ultrasound and FiO_2 needed between newborns that received surfactant and those who didn't.

RDS prevalence is lower at higher gestational age, it can coexist with persistent postnatal lung edema.

LU allows longitudinal evaluation and clearly detects the loss of lung aeration. Eleven patients (34%) with TTN pattern showed $FiO_2 \geq 30\%$ at the time of consultation, and surfactant was being considered. CPAP optimization and pronation (generating net recruitment of the lung in this inhomogeneous pathology) allowed

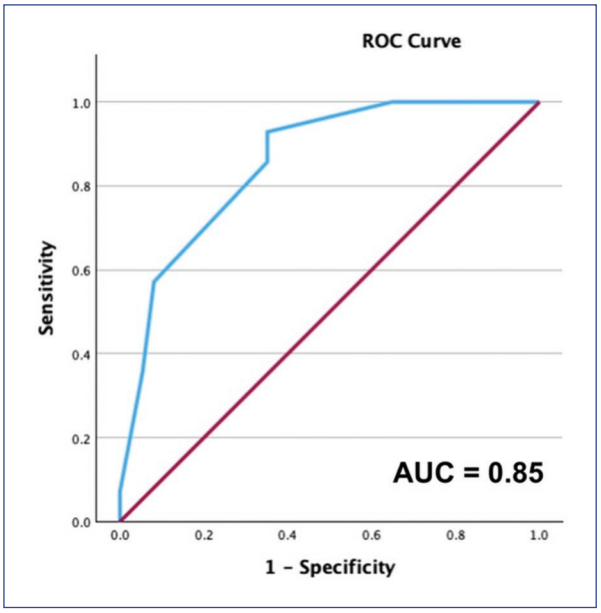

Figure 3. Receiving operator characteristic curve for optimal FiO_2 threshold (24%) to diagnose CPAP failure.

clinical stability and improved gas exchange and lung aeration[25]. Air leak was present in 9% of patients with TTN on first-time consultation and in two patients evaluated for a second dose of surfactant (10%). LU allows a quick and more specific recognition of minor air leaks that might not be evident in traditional CXR and can only be suspected if hypercarbia or worsening of respiratory dynamics acutely presents[26,27].

A network meta-analysis from 2023 found no statistically significant differences between 30%, 40% and 50% FiO_2 thresholds, while the 60% threshold was suggestive of increased morbidity[28]. FiO_2 is a gestational age-dependent predictor of surfactant need, so alternative FiO_2 thresholds have been investigated. More recent studies in centers with LU programs have demonstrated that its accuracy increases when used at lower levels than currently recommended by international guidelines, as low as 23%[8,9]. In our study, a FiO_2 threshold of 24% showed good diagnostic performance to identify CPAP failure.

This study has several limitations. Only the patients consulted at the discretion of the attending neonatal team were included in the study. Ultrasound service was available only Monday-Friday during the morning shift. The strength of this study lies in the analysis of the case series in a perinatal hospital and the advantages shown using LU. To date, there are no similar reports in Mexico. All inferences and analyses were performed by medical personnel trained in neonatology and point-of-care ultrasound by approved programs, and they demonstrate the effects on decision-making.

Conclusion

LU provides very valuable information through pattern recognition and an LUS, allowing differential diagnosis and tailored physiological care. Considering LU as the gold standard for diagnosing CPAP failure, an optimal FiO_2 threshold of 24% with an AUC of 0.85 was found. Pattern recognition allowed CPAP optimization and personalized management of RDS.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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