Medicina Intensiva 50 (2026) 502350

medicina intensiva

http://www.medintensiva.org/en/

UPDATE IN INTENSIVE CARE MEDICINE: PEDIATRIC INTENSIVE CARE

Acute respiratory distress syndrome in the pediatric patient

Susana Reyes-Domínguez[a,*], **Ana Abril-Molina**[b], **Raúl Montero-Yéboles**[c], **Vicente Modesto i Alapont**[d]

[a] *Unidad de Medicina Intensiva Pediátrica, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain*
[b] *Unidad de Medicina Intensiva Pediátrica, Hospital Universitario Virgen de las Nieves, Ibs, Granada, Spain*
[c] *Unidad de Medicina Intensiva Pediátrica, Hospital Universitario Reina Sofía de Córdoba, Córdoba, Spain*
[d] *Unidad de Medicina Intensiva Pediátrica, Hospital Universitari i Politècnic La Fe, Valencia, Spain*

Received 3 April 2025; accepted 13 October 2025
Available online 30 January 2026

KEYWORDS
Pediatric Acute Respiratory Distress Syndrome;
Acute respiratory failure;
Pediatric Acute Lung Injury Consensus Conference;
Respiratory distress;
Mechanical ventilation

Abstract Pediatric acute respiratory distress syndrome (PARDS) is the clinical expression of severe non-cardiogenic pulmonary edema.

The agreed-upon definition shares common criteria with those for adults, but also includes differences determined by the particular characteristics inherent to pediatric patients. The definition of PARDS does not require bilateral infiltrates on the chest X-ray; hypoxemia can be identified non-invasively using the blood oxygen saturation/fraction of inspired oxygen (S/F) ratio; it is stratified into two groups (mild-moderate and severe) after a stabilization period of at least 4 h; and the oxygenation index and the oxygenation-saturation ratio are used in intubated patients.

Optimized respiratory support settings should prevent lung injury and allow for early identification of patients requiring extracorporeal membrane oxygenation (ECMO). This article seeks to conduct a critical analysis of PARS. A precise diagnosis of this syndrome remains challenging.
© 2025 Elsevier España, S.L.U. and SEMICYUC. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

PALABRAS CLAVE
Síndrome de distrés respiratorio agudo pediátrico;
Insuficiencia respiratoria aguda;

Síndrome de distrés respiratorio agudo en el paciente crítico pediátrico

Resumen El síndrome de distrés respiratorio agudo pediátrico (SDRAP) constituye la expresión clínica de un edema pulmonar grave no cardiogénico.

La definición consensuada comparte criterios comunes con la del adulto, pero también diferencias determinadas por la idiosincrasia del niño. La definición del SDRAP no necesita bilateralidad en la radiografía de tórax, se permite identificar la hipoxemia por métodos no invasivos

* Corresponding author.
E-mail address: susanabeatriz.reyes@um.es (S. Reyes-Domínguez).

https://doi.org/10.1016/j.medine.2025.502350
2173-5727/© 2025 Elsevier España, S.L.U. and SEMICYUC. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Conferencia Consenso sobre lesión pulmonar aguda pediátrica; Distrés respiratorio; Ventilación mecánica

con el cociente saturación de oxígeno por pulsioximetría/fracción inspirada de oxígeno (S/F), se estratifica en dos grupos (leve-moderado y grave) tras un periodo de estabilización de al menos 4 horas, y se utiliza el índice de oxigenación (IO) y el índice oxigenación-saturación en pacientes intubados. La programación de un soporte respiratorio optimizado debería evitar la lesión pulmonar y permitir identificar precozmente a los pacientes que requieren oxigenación por membrana extracorpórea (ECMO).

Este artículo busca realizar un análisis crítico sobre el SDRAP. Diagnosticar de forma certera este síndrome es todavía un reto.

© 2025 Elsevier España, S.L.U. y SEMICYUC. Se reservan todos los derechos, incluidos los de minería de texto y datos, entrenamiento de IA y tecnologías similares.

Importance of the problem

Acute respiratory distress syndrome (ARDS) is the clinical expression of pulmonary edema of non-cardiogenic origin. The condition is characterized by a high protein content, heterogeneous involvement, and hypoxemia. The most common risk factors are pneumonia (ARDS of pulmonary origin) and sepsis (ARDS of extrapulmonary origin), but there are other triggering clinical conditions. Secondly, a systemic inflammatory response can damage the alveolar-capillary barrier of the lungs, leading to edema, increased intrapulmonary shunt, and decreased compliance.[1]

The incidence of pediatric acute respiratory distress syndrome (PARDS) is 3.2% (95% confidence interval [95%CI]: 3.0%–3.4%) among patients admitted to the Pediatric Intensive Care Unit (PICU).[2] Mortality is lower than in adults (24%), probably because since acceptance of the application of the SpO_2/FiO_2 (S/F) ratio for the detection of hypoxemia, the diagnosis is established early.[3] The primary cause of mortality is multiorgan failure and neurological disorders. ARDS of extrapulmonary origin is associated with a higher mortality risk.[4]

An as-yet-unvalidated model has been developed to predict ARDS mortality (area under the curve [AUC] = 0.82; 95%CI: 0.78–0.87), using clinical variables recorded on the same day of diagnosis.[5]

Pathophysiology of pediatric acute respiratory distress syndrome

The pathogenesis of ARDS involves inflammatory damage to the pulmonary endothelium and epithelium, which leads to increased vascular permeability at microcirculatory level. The inflammatory cascade generates a protein-rich edema in the pulmonary alveolus and interstitium, even in the presence of normal pulmonary vascular pressure.[1]

The underlying molecular mechanisms are comparable to those observed in adults; however, the overall pulmonary behavior in children may vary due to the presence of an incomplete alveolar structure, the immaturity of the immune system, differences in apoptosis mechanisms that are essential for development and maturation, or the distinct elastic properties of the lungs, particularly in infants.[1]

In the study of pathobiology of PARDS, two subphenotypes with distinct inflammatory and endothelial disorder biomarkers have also been identified: hypoinflammatory and hyperinflammatory. The latter is associated with a higher mortality rate and concomitant sepsis.[6,7] The model identifying the hyperinflammatory subphenotype considers the use of vasopressors and elevated levels of endothelial disorder (AGN-2) and inflammatory biomarkers such as interleukins (IL) IL-6, CCL3, and IL-8. It has a sensitivity [S] of 0.75 and 0.93, respectively, and a precision of 0.88, with an AUC of 0.93 (95%CI: 0.90–0.97). Further research is necessary to ascertain its practical applications.[8]

Definition of pediatric acute respiratory distress syndrome

Diagnosis of pediatric acute respiratory distress syndrome

The consensuses on adult ARDS (American-European Consensus Conference,[9] Berlin[10]) and the Pediatric Acute Lung Injury Consensus Conference (PALICC and PALICC-2)[11,12] both agree on the diagnosis of adult acute respiratory distress syndrome (ARDS). However, there are also some important differences in the diagnostic criteria for pediatric patients due to the particular characteristics inherent to the pediatric patient.

According to the most recent pediatric consensus,[12] PARDS is defined as a set of symptoms of hypoxemia and radiological changes that appear within seven days after pulmonary or extrapulmonary disease. This includes cases of pulmonary edema that cannot be fully explained by heart failure, volume overload, and/or perinatal respiratory disease (Table 1). A recent consensus among adults[13] categorizes patients into three groups: non-intubated (including high-flow oxygen therapy [HFOT]), intubated, and resource-poor scenarios. The utilization of S/F in the absence of PaO_2/FiO_2 (P/F) is proposed to assess oxygenation, and lung ultrasound can be employed for radiological imaging (Table 2).

The diagnosis of PARDS does not require bilateral involvement on the chest X-ray. Rather, it is characterized by the presence of new opacities in the lung parenchyma that are

Table 1 Definition of Pediatric Acute Respiratory Distress Syndrome according to the Pediatric Acute Lung Injury Consensus Conference.[12]

Age	Exclusion of perinatal lung disease		
Time	Acute onset within 7 days of a known clinical event		
Edema	Not explained by HF or fluid overload		
Chest Rx	New parenchymal opacities, rule out atelectasis and pleural effusion		
Oxygenation	NIV: P/F $\leq$ 300 or S/F $\leq$ 250 (facial or oronasal interface with a CPAP/EPAP $\geq$ 5 cmH_2O) IMV: OI $\geq$ 4 or OSI $\geq$ 5		
	Stratification of ARDS severity after $\geq$ 4 h of diagnosis:		
	PARDS	Mild/Moderate	Severe
	IMV-PARDS	OI < 16 or OSI < 12	OI $\geq$ 16 or OSI $\geq$ 12
	NIV-PARDS	P/F > 100 or S/F > 150	P/F $\leq$ 100 or S/F $\leq$ 150

PARDS: pediatric acute respiratory distress syndrome; HF: heart failure; NIV: noninvasive ventilation; P/F: partial pressure of oxygen/inspired oxygen fraction; Rx: chest X-ray; S/F: oxygen saturation measured by pulse oximetry/inspired oxygen fraction; IMV: invasive mechanical ventilation; OI: oxygenation index ([FIO_2 $\times$ mean airway pressure $\times$ 100]/PaO_2); OSI: oxygenation saturation index ([FIO_2 $\times$ mean airway pressure $\times$ 100]/SpO_2) CPAP: continuous positive airway pressure; EPAP: expiratory positive airway pressure.

Table 2 Diagnostic accuracy of ARDS definitions.

		BERLIN adults	PALICC
Patients		Adults	Children with MV
Experimental design		Retrospective cohort	Prospective cohort
Results	Sensitivity	94% (95% CI: 89%–97%)	92.6% (95% CI: 81.4%–95.2%)
	Specificity	46% (95% 95%: 40%–52%)	88.3% (CI: 86%–89%)
	Weight of positive evidence (decibans)	2.41 (95% CI: 1.71%–3.06%)	8.95 (95% CI: 8.04%–9.84%)
	Weight of negative evidence (decibans)	−8.85 (95% CI: −5.61 to 12.39)	−10.8 (95% CI: −17 to 6.75)

NA: not applicable; MV: mechanical ventilation; CI: confidence interval.
Modified from Ref.[80]

not explained by atelectasis or pleural effusions. The consideration of this clinical criterion has not increased the diagnosis of PARDS, as 87% of these patients exhibit bilateral infiltrates within three days.[2] Conversely, chest radiography is susceptible to significant interobserver variability, even when interpreting the number of affected quadrants. Research indicates that patients with infiltrates in all four quadrants and a large intrapulmonary shunt (P/F < 100) have a high mortality rate.[14] In summary, oxygenation levels offer a more objective measurement of severity in PARDS cases than radiological imaging.

The methodology used in the radiographic assessment of lung edema (RALE) score developed by Yan et al. in PARDS attempts to more objectively delineate the lung quadrants and parenchymal density.[15] However, it remains imprecise.

The PALICC-2 definition has been shown to have equivalent mortality predictive capacity in pediatric patients as the Berlin definition. Its prognostic ability increases the longer the time elapsed since the onset of the disease.[16] Therefore, it is an effective predictor of mortality on the third day (odds ratio [OR], 256.5, 95% confidence interval [95%CI]: 27.1–2.424, P < .001), with an oxygenation index (OI) cut-off value of 17 (AUC = 0.92 [95%CI = 0.83–1], S 0.97; specificity [E] 0.87; P = .0001).[17]

In terms of diagnostic accuracy, if a patient meets the PALICC-2 criteria, the probability of PARDS increases almost ninefold. Conversely, if the patient does not meet the established criteria, the probability decreases to less than 10%.[18–20]

Furthermore, the diagnosis of PARDS is accepted in patients with congenital heart disease or chronic lung disease, even if severity stratification using the hypoxemia criteria is not feasible.

''Possible'' pediatric acute respiratory distress syndrome

This new category includes those patients receiving non-invasive nasal respiratory support in the context of non-invasive ventilation (NIV) with bi-level positive airway pressure (BiPAP), nasal continuous positive airway pressure (nasal CPAP), or HFO $\geq$ 1.5 l/kg/m or $\geq$30 l/m. This category permits the exclusion of the radiological criterion in settings with limited medical resources, provided that the other criteria are met.[12]

Patient ''at risk'' for pediatric acute respiratory distress syndrome

These are patients who receive oxygen to maintain SpO2 $\geq$ 88%, but do not meet the definition of PARDS or ''possible PARDS''. This category is instrumental in evaluating disease progression and implementing prevention strategies.

Severity stratification

It is essential to stratify patients based on severity at least four hours after the diagnosis of ARDS. Two prognostic categories are described: mild-moderate oxygenation index (OI) < 16 or severe OI ≥ 16.[12]

For patients on invasive mechanical ventilation (IMV), the OI should be calculated as F × mean airway pressure (MAP) × 100/P, and the oxygenation-saturation index (OSI) as F × MAP/S. For patients on non-invasive ventilation (NIV), the P/F ratio or S/F should be used. The selection of P/F for severity stratification is based on a study that compared intrapulmonary shunt measured with clinical parameters (P/F) and the translation into lung density on the CT scan of adult patients with ARDS.[21] However, OI and OSI do not convey this meaning. MAP, included in both formulas, can be modified by several parameters that do not influence oxygenation, such as inspiratory time or the I:E ratio.[22,23] Therefore, given that positive end-expiratory pressure (PEEP) and not MAP is associated with lung recruitment, and since it does not measure the degree of intrapulmonary shunt, the use of OI and OSI could be called into question. However, studies have been conducted using the P/F ratio as the gold standard for diagnosing ARDS. For example, a study by Thomas et al. reported a high accuracy of OI and the S/F ratio, although not of OSI.[24]

The use of the S/F ratio as a marker of lung damage is very useful in pediatrics, since sedation and cannulation of an arterial access can have a detrimental effect on the patient's baseline condition. Therefore, non-invasive monitoring is ideal in patients with mild-moderate involvement and subjected to NIV. Such measurement should be performed under stable conditions and not during transient desaturation episodes. To find the area of the hemoglobin dissociation curve where the linear relationship between P/F and S/F is found, we must adjust FiO_2 to maintain $SpO_2 \leq 97\%$.[25,26]

Treatment

To date, no pharmacological treatment has demonstrated efficacy in the management of ARDS. The primary objective of respiratory support is to ensure adequate oxygen delivery to the tissues while preventing ventilator-induced lung injury (VILI).

The identification of the mechanical factors that induce greater lung injury has influenced the decrease in mortality. The type of support provided should align with the severity of hypoxemia (Fig. 1).

Respiratory support in non-invasive ventilation

Multicenter studies have generated controversy in the use of NIV in PARDS. The main point of debate is the selection of responders, since a delay in intubation, self-inflicted NIV injury or even the methodology of use, can influence the results.[27]

To classify the severity of PARDS, it is necessary to administer NIV through a full face mask or oronasal mask, either CPAP or BiPAP.

Although NIV in the pediatric patient has reduced the duration of ventilation and the number of severe complications related to IMV even in hypoxemic disease,[28] several studies have described that NIV support worsens the prognosis in PARDS, even in immunocompromised children.[29,30] Furthermore, on controlling for potential confounders in a propensity score analysis, it was seen that regardless of the severity of PARDS, the following are risk factors for NIV failure: severity of hypoxemia, immunosuppression status, the male sex, and a non-respiratory Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score > 2. For this reason, extreme caution should be exercised when using NIV in these patients.[31]

The S/F ratio identifies NIV responders, and S/F > 200 correlates well with P/F > 200.[32] Its application for identifying the most severely ill patients also appears promising.[33] Therefore, if there is insufficient improvement in respiratory distress, heart rate or PaO_2/FiO_2 or SpO_2/FiO_2 ratio during the first 6 h of NIV support, intubation and IMV should be performed.[2,34] In patients with compromised immune systems or multiple organ failure, or in cases of moderate-to-severe acute respiratory distress syndrome (ARDS), the decision to intubate should be made within the first two hours after initiating non-invasive ventilation (NIV). The impact of patient length of stay on NIV before intubation on the severity of the prognosis is a subject of ongoing discussion. A pediatric study found no association between the duration of NIV before intubation, the duration of IMV, or the duration of admission.[35] For mild-moderate cases on NIV, it is advisable to undergo continuous monitoring in the PICU to avoid delaying intubation.[36]

It is considered good practice to administer sedation during NIV to promote synchronization, titrating the dose to maintain protective airway reflexes and spontaneous respiratory mechanics.[37]

To ensure the optimal performance of NIV,[27] it is essential to prioritize humidification, select the appropriate interface, and monitor for complications.

Lung protection strategies in invasive mechanical ventilation

It is recommended that lung protection strategies include the adjustment of tidal volume (Vt), plateau pressure (Pplat), driving pressure (DP), and PEEP. These measures should be used within recommended limits to prevent VILI (Table 4). In addition to the classical mechanisms (atelectrauma, volutrauma, biotrauma), materials engineering is applied to describe VILI. Mechanical power (MP) is defined as the energy transmitted by the ventilator to the respiratory system per unit of time. It establishes the relationship between the effort or tension (stress) supported by the lung and the deformation (strain) induced in it by the applied force. MP increases exponentially with Vt, DP, flow, and respiratory frequency, and increases linearly with PEEP and airway resistance (Raw). These variables are described as factors associated with mortality in ventilated patients.[38]

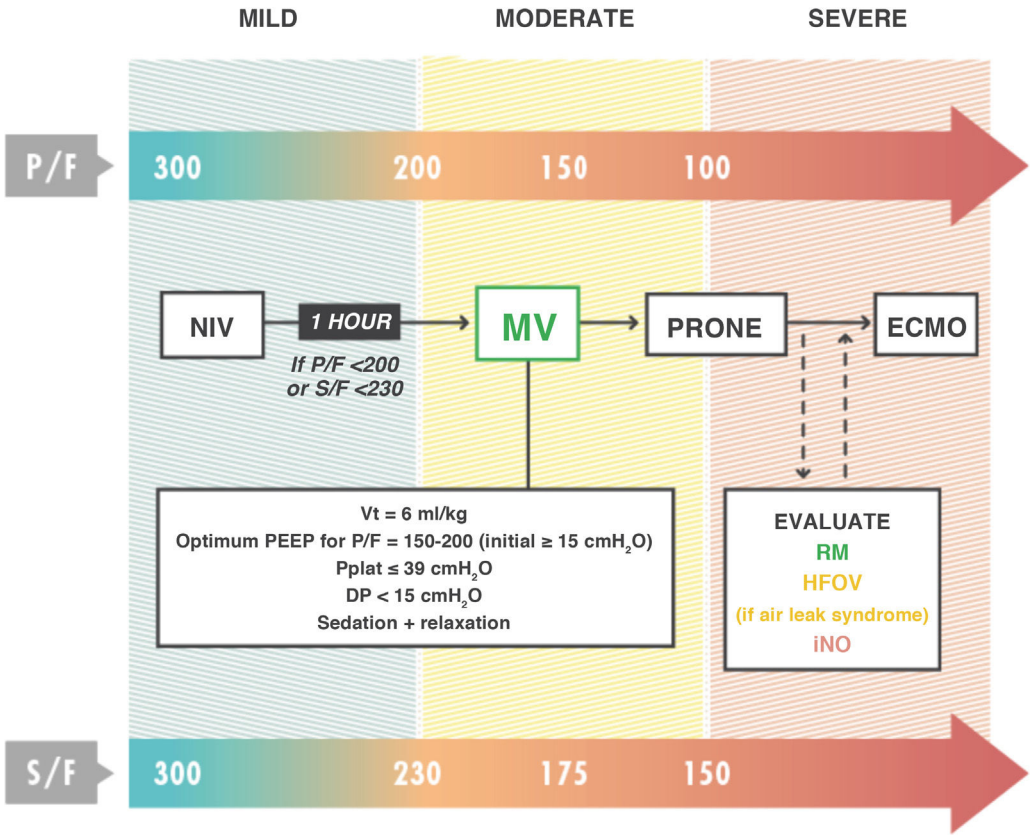

Figure 1 Diagnostic and therapeutic scheme applicable to acute respiratory distress syndrome (ARDS).
ECMO: extracorporeal membrane oxygenation; RM: recruitment maneuvers; iNO: inhaled nitric oxide; P/F: partial arterial pressure of oxygen/inspired oxygen fraction; S/F: oxygen saturation measured by pulse oximetry/inspired oxygen fraction; HFOV: high frequency oscillatory ventilation; MV: mechanical ventilation; NIV: non-invasive ventilation.
Reproduced from Ref.[80]

Ventilation mode

At this time, there is no evidence to recommend pressure or volume ventilation in patients with PARDS. Similarly, high-frequency oscillatory ventilation is not recommended except when the ventilatory and oxygenation goals are not achieved after optimizing the lung protection strategy in conventional modalities.[12]

Optimal positive end-expiratory pressure

The application of optimal PEEP aims to keep as many alveolar units as possible ''open'' throughout the respiratory cycle.[39] This strategy is aimed at reducing intrapulmonary shunt and ensuring sufficient gas exchange. PEEP titration should be performed on an individualized basis, with close monitoring of the effect on P/F, OI, compliance, and hemodynamics.[40] At present, the table proposed in the ARDS Network protocol is recommended, where a PEEP level in relation to FiO_2 is selected as a starting point (Table 3).[12] It has been demonstrated that there is a higher mortality rate in children who received less PEEP than the amount indicated in this table. Conversely, a PEEP level that exceeded the recommended range by up to 5 cmH_2O did not increase mortality.[41]

The Open Lung Strategy (OLS), which includes high PEEP levels and low tidal volume, is considered the gold standard for adult patients with ARDS. However, studies have not demonstrated a reduction in mortality with this strategy. The latter may be particularly advantageous for patients who have not been successfully recruited by conventional methods (P/F < 150) and for whom applying a higher PEEP results in reduced energy application to the lung (i.e., decreasing DP or MP).[38]

Tidal volume, plateau pressure, and distending pressure

Although the level of evidence is low, ventilation with a tidal volume (Vt) of 6–8 ml/kg is recommended. It may be necessary to adjust Vt to below 6 ml/kg to avoid exceeding the Pplat or DP limits. However, it is important to note that volumes lower than 4 ml/kg have been associated with an increased mortality rate.[27] The calculations should be based on the lowest weight (ideal or actual).[12]

In the adult population, studies have demonstrated that limiting Pplat significantly reduces mortality. A Cochrane systematic review indicates that for a Pplat below 32 cmH_2O, there is no observed difference in mortality rates for ARDS. However, given the absence of pediatric studies in

Table 3 FiO_2/PEEP based on ARDSnet (low PEEP/high FiO_2).[12]

FiO_2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
PEEP cmH_2O	5	6–8	8–10	10	10–14	14	14–18	18–24

FiO_2: oxygen concentration; PEEP: positive end-expiratory pressure; ARDSnet: respiratory distress syndrome working group.

Table 4 Main parameters and limits recommended for applying a protective ventilation strategy in the pediatric ARDS patient.

Ventilatory strategy in ARDS	
Main parameters to be programmed	Recommended limit
Vt: 6 ml/kg	8 ml/kg
PEEP: titrate	Pplat control, static compliance and DP
Minimum FiO_2 for SpO_2 targets:	<60%
- Mild-moderate ARDS 92%–97%	
- Severe ARDS 88%–92%*	
Parameters to monitor	
Pplat (static)	<28–32 cmH_2O
Static DP = Pplat-PEEP	<15 cmH_2O

Pplat: plateau pressure; DP: driving pressure.
* If SpO_2 < 92%, central SvO_2 monitoring should be used, and oxygen transport/consumption should be monitored.

this regard, it is advisable to limit Pplat to 28 cmH_2O, allowing up to 32 cmH_2O in patients with low compliance, as well as DP < 15 cmH_2O.[42]

Oxygenation and homeostasis objectives

Although the evidence is insufficient, the PALICC-2 guidelines recommend maintaining SpO_2 ranges between 92%–97%. In critically ill patients, SpO_2 levels between 88%–92% are considered acceptable, but central venous saturation and other indicators related to oxygen transport and consumption should be closely monitored.

With regard to the permissive hypercapnia strategy (with pH > 7.20), it may be necessary to maintain protective ventilation, and its application has been shown to reduce mortality in pediatric patients.[3] Greater control is indicated in disorders such as intracranial hypertension, severe pulmonary hypertension, some congenital heart diseases, and/or patients with severe ventricular dysfunction and/or hemodynamic instability. Conversely, the administration of bicarbonate is recommended exclusively in severe metabolic acidosis or pulmonary hypertension with severe cardiac and hemodynamic involvement.[43]

Extracorporeal membrane oxygenation support

In the case of adult patients with very severe ARDS (P/F 75), the use of extracorporeal membrane oxygenation (ECMO) in the first 48 h has been shown to significantly reduce the probability of death or severe disability at 6 months. The number of patients needed to treat (NNT) to achieve this outcome is four (relative risk [RR] 0.65; 95%CI: 0.52–0.80) (Table 5). In addition, it has proven to be cost-effective. To date, pediatric studies on mortality in ARDS patients undergoing ECMO, although limited, show scientific evidence of its benefit.[44]

Table 5 Number of patients that need to be treated to benefit from ARDS treatments.

Treatment used	Estimated NNT
Corticosteroids	12 (RR 0.82; 95%CI: 0.72–0.95)
Prone position	6 (RR 0.69; 95%CI: 0.48–0.99)
Neuromuscular blockade	6 (RR 0.65; 95%CI: 0.51–0.84)
ECMO	4 (RR 0.65; 95%CI: 0.52–0.80).
Inhaled nitricoxide	Not applicable

NNT: needed to treat; ARDS: acute respiratory distress syndrome; ECMO: extracorporeal membrane oxygenation.

In children, there is currently no evidence to support the use of strict criteria for selecting patients who will benefit from ECMO. Veno-venous (VV) ECMO should be considered as a rescue strategy for patients with refractory hypoxemia, following a structured evaluation by an expert team, when other treatment options have failed, including fluid restriction, prone positioning, and protective ventilation.[45]

Research has demonstrated that patients receiving VV ECMO exhibit enhanced hemodynamic stability and reduced reliance on vasoactive medications.[46] Therefore, the choice of the type of assistance should be based not only on the necessity for vasoactive drugs[47] but also on the presence of cardiac dysfunction. In the event of recovery, early conversion to VV ECMO is a viable option.[48] During ECMO therapy, close monitoring is essential, and the necessity for veno-arterial (VA) ECMO should be assessed in cases of right ventricular failure.[49] The survival rate is higher in patients undergoing VV ECMO compared to VA ECMO.[50]

The most common complications of VV ECMO are bleeding (29.3%), neurological complications (7.1%), including intracranial hemorrhage, ischemic stroke, brain death, and seizures.[47]

In the initial stages of extracorporeal support, it is essential to avoid hyperoxia and instead induce a gradual decrease in the partial pressure of CO_2. This approach is crucial to prevent neurological complications, as abrupt decreases have been associated with an increased risk for such complications.[47] The initiation of ECMO typically results in a reduction of ventilator parameters to protective levels. Even when adequate support is provided, extubation of the patients is considered as they recover from pulmonary complications. Pediatric studies have reported increased mortality in those patients with greater FiO_2, Pplat, and DP or with Vt < 4 ml/kg during ECMO support.[51,52] Therefore, lung protection measures should be maintained

(Pplat < 28–32 cmH_2O, DP < 15 cmH_2O, and general reduction of MP).[53]

A recent study has indicated that the prone position during ECMO does not appear to offer any advantages in terms of reducing the duration of support when compared to the supine position.[54]

Other support measures

Prone ventilation

Prone ventilation is regarded as a primary strategy for severe ARDS in adult patients. It is a lung protective measure that enhances compliance, gas exchange, and overall lung mechanics. If performed within 36 h of diagnosis and for a minimum of 16 h per day, there is a reduced risk of mortality.[54]

While the data are insufficient in pediatrics, its use is considered to optimize recruitment in patients who could not be recruited by other means (P/F < 150).[55] Given the current evidence, it is not possible to specify the length of time the pediatric patient should remain prone.[56]

Improvement of the ventilation-perfusion ratio has been observed in patients with PARDS undergoing prone ventilation and studied using electrical impedance tomography.[57] However, the temporary enhancement in oxygenation did not result in a substantial decrease in mechanical ventilation duration.[58–60] A multicenter study is currently underway to clarify the benefits of this practice.[61]

Recruitment maneuvers

There is insufficient evidence to recommend the application of recruitment maneuvers (RM) in pediatrics. Recruitment maneuvers consist of transient increases in insufflation pressure to open collapsed alveolar units, followed by fine-tuning of PEEP to the optimal level (P/F > 150–175), since reaching higher P/F values may increase MP and, therefore, mortality.

In adult patients with diffuse lesions, a tendency to hyperinsufflation of well-ventilated areas has been observed in those with patchy lesions.[62] Conversely, deleterious effects were observed with RM with progressive increases in PEEP of 5 cmH_2O.[63]

In selected pediatric patients with severe PARDS, slow incremental or decremental PEEP changes (typically PEEP steps of 2 cmH_2O) can be made while continuously monitoring the patient's oxygenation, compliance, and hemodynamics. It is not advisable to implement sustained insufflation maneuvers in children. To date, there are no studies that establish the mode of application, safety, and usefulness of RM. The implementation of point-of-care ultrasound has the potential to enhance the safety of these maneuvers.[64]

Inhaled nitric oxide

The PALICC considers that inhaled nitric oxide (iNO) cannot be routinely advised in children with ARDS but can be recommended in selected cases. It produces a transient improvement in oxygenation, but does not reduce mortality, and increases the risk of renal failure.[65]

The concentrations of iNO reaching the alveolus depend on two factors: the type of device used for administration and the mode of delivery of the gas into the lungs.[66]

An iNO test is acceptable when there is suspicion of other shunt mechanisms contributing to poor oxygenation (altered hypoxic pulmonary vasoconstriction, pulmonary hypertension in patients with patent foramen ovale). These cases are very prevalent in pediatrics (bronchiolitis, viral pneumonias, etc.).[67] The use of iNO is also considered in patients with documented pulmonary hypertension or severe right ventricular dysfunction.[12]

A pediatric clinical trial was unable to demonstrate improvement in mortality; however, the use of iNO reduced the need for ECMO in PARDS.[68] If it is not effective, it should be withdrawn within 4 h in order to avoid side effects.

Other recommendations

Muscle relaxation and sedoanalgesia

The application of scales to monitor pain, sedation, withdrawal, and delirium is recommended as a good clinical practice standard.[69]

The use of minimal effective sedation is crucial to ensure the successful implementation of the ventilatory strategy. Drug dose titration should be performed with specific objectives, such as facilitating mobility and some activity, while also ensuring the promotion of quality sleep during the nighttime hours. In regard to delirium, it is essential to perform daily assessments utilizing validated pediatric scales. It is crucial to note that delirium cannot be detected in states of deep sedation (State Behavioral Scales ≤ 2 points).[69]

The administration of muscle relaxants is recommended if adequate sedoanalgesia is insufficient to maintain protective ventilation. The dosage should be titrated, administering the minimum effective dose, and if possible, by means of the train of four.[69]

Care of the airway

For patients with PARDS, the intubation process should be performed electively using cuffed endotracheal tubes (ETT) to prevent de-recruitment.[55] ETT with subglottic secretion drainage, from size 6.0 and above, is an option for patients over 10 years of age.[70]

There is no difference in morbidity and mortality with respect to the choice between programmed or necessary aspirations. It is imperative that suction catheters be positioned such that they occlude less than 70% of the ETT lumen. Furthermore, it is crucial to maintain suction pressure below −120 mmHg. Deep aspiration should be performed only when superficial suctioning proves ineffective. The FiO_2 required for preoxygenation should be titrated, and saline instillation should be avoided.[71]

Water balance and nutrition

Although there is little evidence to support it, a pediatric clinical trial found that restricting fluid during the resuscitation phase and reducing total body fluid balance thereafter improved the number of days without mechanical ventilation (MV-free days) compared to the liberal strategy.[72] Furthermore, volume overload $\geq$ 5% within the first 24 h of admission has been associated with a higher risk of acute renal failure and prolonged IMV.[73]

It is important to note that different ARDS phenotypes may respond differently to fluid management, and focused studies are needed to determine the most effective approach.[74]

Given its protective role, the start of enteral nutrition within the first 72 h is recommended. In addition, the administration of at least 1.5 g/kg/day of protein per day is necessary to ensure a positive protein balance. Similarly, it is advisable to maintain a nutrition plan that addresses metabolic requirements, promotes recovery, and facilitates sustained growth.[75]

Transfusions

Transfusion is not recommended if the patient has a hemoglobin level of at least 7 g/dl, unless there is hemodynamic instability, baseline chronic cyanotic disease, severe ARDS, or hemolytic anemia.[75]

Corticosteroids and surfactant

For adult patients with ARDS due to SARS-CoV-2, corticosteroid treatment is considered a standard treatment option.[76] In the field of pediatrics, there is currently no evidence to support the use of corticosteroids or surfactant administration in cases of PARDS.[77]

Long-term evolution

In terms of evolution and prognosis, it is advisable to promote early weaning from MV in order to reduce complications. Barajas-Romero et al. defined prolonged ventilation after analyzing the diagnoses and treatments used, setting a cut-off point of nine days.[78]

The most common acquired morbidity in survivors primarily affects the respiratory system and feeding (dysphagia). Rehabilitation programs must prioritize these domains, while simultaneously recognizing the profound impact of the disease and its complications on the neurodevelopment of the child.[79]

CRediT authorship contribution statement

All authors have played an active role in the drafting and revision of the manuscript. They therefore assume responsibility for the content presented and guarantee that it faithfully reflects the bibliography used.

Financial support

No funding has been received for this article.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

References

1. Heidemann SM, Nair A, Bulut Y, Sapru A. Pathophysiology and management of acute respiratory distress syndrome in children. Pediatr Clin North Am. 2017;64:1017–37, http://dx.doi.org/10.1016/j.pcl.2017.06.004.
2. Khemani RG, Smith L, Lopez-Fernandez YM, Kwok J, Morzov R, Klein MJ, et al. Paediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE): an international, observational study. Lancet Respir Med. 2019;7:115–28, http://dx.doi.org/10.1016/S2213-2600(18)30344-8.
3. Wong JJM, Lee SW, Tan HL, Ma Y-J, Sultana R, Mok YH, et al. Lung-protective mechanical ventilation strategies in pediatric acute respiratory distress syndrome. Pediatr Crit Care Med. 2020;21:720–8, http://dx.doi.org/10.1097/PCC.0000000000002324.
4. Meyer NJ, Gattinoni L, Calfee CS. Acute respiratory distress syndrome. Lancet. 2021;398(10300):622–37, http://dx.doi.org/10.1016/S0140-6736(21)00439-6.
5. Yehya N, Harhay MO, Klein MJ, Shein SL, Piñeres-Olave BE, Izquierdo L, et al. Predicting mortality in children with pediatric acute respiratory distress syndrome: a pediatric acute respiratory distress syndrome incidence and epidemiology study. Crit Care Med. 2020;48:e514–522, http://dx.doi.org/10.1097/CCM.0000000000004345.
6. Yehya N, Zinter MS, Thompson JM, Lim MJ, Hanudel MR, Alkhouli MF, et al. Identification of molecular subphenotypes in two cohorts of paediatric ARDS. Thorax. 2024;79:128–34, http://dx.doi.org/10.1136/thorax-2023-220130.
7. Dahmer MK, Yang G, Zhang M, Quasney MW, Sapru A, Weeks HM, et al. Identification of phenotypes in paediatric patients with acute respiratory distress syndrome: a latent class analysis. Lancet Respir Med. 2022;10:289–97, http://dx.doi.org/10.1016/S2213-2600(21)00382-9.
8. Zurawel AA, Coates BM. Time to split: biomarker trajectories in pediatric acute respiratory distress syndrome hint at underlying disease. J Clin Invest. 2024;134:e180662, http://dx.doi.org/10.1172/JCI180662.
9. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med. 1994;149:818–24, http://dx.doi.org/10.1164/ajrccm.149.3.7509706.
10. Ranieri M, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome. JAMA. 2012;307:2526–33, http://dx.doi.org/10.1001/jama.2012.5669.
11. Jouvet P, Thomas NJ, Wilson DF, Erickson S, Khemani R, Zimmerman J, et al. Pediatric acute respiratory distress syndrome. Pediatr Crit Care Med. 2015;16:428–39, http://dx.doi.org/10.1097/PCC.0000000000000350.
12. Emeriaud G, López-Fernández YM, Iyer NP, Bembea MM, Agulnik A, Barbaro RP, et al. Executive summary of the Second International Guidelines for the Diagnosis and Management of Pediatric Acute Respiratory Distress Syndrome (PALICC-2). Pediatr Crit Care Med. 2023;24:143–68, http://dx.doi.org/10.1097/PCC.0000000000003147.

13. Matthay MA, Arabi Y, Arroliga AC, Bernard G, Bersten AD, Brochard LJ, et al. A new global definition of acute respiratory distress syndrome. Am J Respir Crit Care Med. 2024;209:37–47, http://dx.doi.org/10.1164/rccm.202303-0558WS.
14. López-Fernández YM, Smith LS, Kohne JG, Weinman JP, Modesto-Alapont V, Reyes-Dominguez SB, et al. Prognostic relevance and inter-observer reliability of chest-imaging in pediatric ARDS: a pediatric acute respiratory distress incidence and epidemiology (PARDIE) study. Intensive Care Med. 2020;46:1382–93, http://dx.doi.org/10.1007/s00134-020-06074-7.
15. Yan Y-C, Hao W-H, Bai F-S, Liu S, Qu D, Yuan X-Y. Clinical outcome discrimination in pediatric ARDS by chest radiograph severity scoring. Can Respir J. 2022;2022:1–6, http://dx.doi.org/10.1155/2022/9309611.
16. Yehya N, Servaes S, Thomas NJ. Characterizing degree of lung injury in pediatric acute respiratory distress syndrome. Crit Care Med. 2015;43:937–46, http://dx.doi.org/10.1097/CCM.0000000000000867.
17. Rsovac S, Milošević K, Plavec D, Todorović D, Šćepanović L. Third-day oxygenation index is an excellent predictor of survival in children mechanically ventilated for acute respiratory distress syndrome. Risk Manag Healthc Policy. 2020;13:1739–46, http://dx.doi.org/10.2147/RMHP.S253545.
18. Thille AW, Esteban A, Fernández-Segoviano P, Rodriguez J-M, Aramburu J-A, Peñuelas O, et al. Comparison of the Berlin definition for acute respiratory distress syndrome with autopsy. Am J Respir Crit Care Med. 2013;187:761–7, http://dx.doi.org/10.1164/rccm.201211-1981OC.
19. De Luca D, Piastra M, Chidini G, Tissieres P, Calderini E, Essouri S, et al. The use of the Berlin definition for acute respiratory distress syndrome during infancy and early childhood: multicenter evaluation and expert consensus. Intensive Care Med. 2013;39:2083–91, http://dx.doi.org/10.1007/s00134-013-3110-x.
20. Rudolph M, van Dijk J, de Jager P, Dijkstra SK, Burgerhof JGM, Blokpoel RGT, et al. Performance of acute respiratory distress syndrome definitions in a high acuity paediatric intensive care unit. Respir Res. 2021;22:256, http://dx.doi.org/10.1186/s12931-021-01848-z.
21. Reske AW, Costa ELV, Reske AP, Rau A, Borges JB, Beraldo MA, et al. Bedside estimation of nonaerated lung tissue using blood gas analysis*. Crit Care Med. 2013;41:732–43, http://dx.doi.org/10.1097/CCM.0b013e3182711b6e.
22. Mercat A, Richard J-CM, Vielle B, Jaber S, Osman D, Diehl J-L, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome. JAMA. 2008;299:646, http://dx.doi.org/10.1001/jama.299.6.646.
23. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med. 2004;351:327–36, http://dx.doi.org/10.1056/NEJMoa032193.
24. Thomas NJ, Shaffer ML, Willson DF, Shih M-C, Curley MAQ. Defining acute lung disease in children with the oxygenation saturation index*. Pediatr Crit Care Med. 2010;11:12–7, http://dx.doi.org/10.1097/PCC.0b013e3181b0653d.
25. Khemani RG, Thomas NJ, Venkatachalam V, Scimeme JP, Berutti T, Schneider JB, et al. Comparison of SpO2 to PaO2 based markers of lung disease severity for children with acute lung injury*. Crit Care Med. 2012;40:1309–16, http://dx.doi.org/10.1097/CCM.0b013e31823bc61b.
26. Parvathaneni K, Belani S, Leung D, Newth CJL, Khemani RG. Evaluating the performance of the pediatric acute lung injury consensus conference definition of acute respiratory distress syndrome*. Pediatr Crit Care Med. 2017;18:17–25, http://dx.doi.org/10.1097/PCC.0000000000000945.
27. Carroll CL, Napolitano N, Pons-Òdena M, Iyer NP, Korang SK, Essouri S. Noninvasive respiratory support for pediatric acute respiratory distress syndrome: from the Second Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med. 2023;24 Supplement 1 2S:S135–147, http://dx.doi.org/10.1097/PCC.0000000000003165.
28. Morris JV, Ramnarayan P, Parslow RC, Fleming SJ. Outcomes for children receiving noninvasive ventilation as the first-line mode of mechanical ventilation at intensive care admission: a propensity score-matched cohort study*. Crit Care Med. 2017;45:1045–53, http://dx.doi.org/10.1097/CCM.0000000000002369.
29. Kopp W, Gedeit RG, Asaro LA, McLaughlin GE, Wypij D, Curley MAQ. The impact of preintubation noninvasive ventilation on outcomes in pediatric acute respiratory distress syndrome*. Crit Care Med. 2021;49:816–27, http://dx.doi.org/10.1097/CCM.0000000000004819.
30. Lemiale V, Resche-Rigon M, Mokart D, Pène F, Rabbat A, Kouatchet A, et al. Acute respiratory failure in patients with hematological malignancies: outcomes according to initial ventilation strategy. A groupe de recherche respiratoire en réanimation onco-hématologique (Grrr-OH) study. Ann Intensive Care. 2015;5:28, http://dx.doi.org/10.1186/s13613-015-0070-z.
31. Emeriaud G, Pons-Òdena M, Bhalla AK, Shein SL, Killien EY, Modesto i Alapont V, et al. Noninvasive Ventilation for pediatric acute respiratory distress syndrome: experience from the 2016/2017 Pediatric Acute Respiratory Distress Syndrome Incidence and Epidemiology Prospective Cohort Study*. Pediatr Crit Care Med. 2023;24:715–26, http://dx.doi.org/10.1097/PCC.0000000000003281.
32. Lobete C, Medina A, Rey C, Mayordomo-Colunga J, Concha A, Menéndez S. Correlation of oxygen saturation as measured by pulse oximetry/fraction of inspired oxygen ratio with Pao2/fraction of inspired oxygen ratio in a heterogeneous sample of critically ill children. J Crit Care. 2013;28:538.e1–7, http://dx.doi.org/10.1016/j.jcrc.2012.12.006.
33. Brown SM, Duggal A, Hou PC, Tidswell M, Khan A, Exline M, et al. Nonlinear imputation of Pao 2/Fio 2 from Spo 2/Fio 2 among mechanically ventilated patients in the ICU: a prospective, observational study. Crit Care Med. 2017;45:1317–24, http://dx.doi.org/10.1097/CCM.0000000000002514.
34. Mayordomo-Colunga J, Pons M, López Y, José Solana M, Rey C, Martínez-Camblor P, et al. Predicting non-invasive ventilation failure in children from the SpO2/FiO2 (SF) ratio. Intensive Care Med. 2013;39:1095–103, http://dx.doi.org/10.1007/s00134-013-2880-5.
35. Bustos-Gajardo FD, Luarte-Martínez SI, Dubo Araya SA, Adasme Jeria RS. Clinical outcomes according to timing to invasive ventilation due to noninvasive ventilation failure in children. Med Intensiva (Engl Ed). 2023;47:65–72, http://dx.doi.org/10.1016/j.medine.2021.10.013.
36. Fernández A, Modesto V, Rimensberger PC, Korang SK, Iyer NP, Cheifetz IM. Invasive ventilatory support in patients with pediatric acute respiratory distress syndrome: from the second pediatric acute lung injury consensus conference. Pediatr Crit Care Med. 2023;24 Supplement 1 2S:S61–75, http://dx.doi.org/10.1097/PCC.0000000000003159.
37. Bermúdez-Barrezueta L, Mayordomo-Colunga J, Miñambres-Rodríguez M, Reyes S, Valencia-Ramos J, Lopez-Fernandez YM, et al. Implications of sedation during the use of noninvasive ventilation in children with acute respiratory failure (SEDANIV Study). Crit Care. 2024;28:235, http://dx.doi.org/10.1186/s13054-024-04976-2.
38. Modesto i Alapont V, Medina Villanueva A, del Villar Guerra P, Camilo C, Fernández-Ureña S, Gordo-Vidal F, et al. OLA strategy for ARDS: its effect on mortality depends on achieved recruitment (PaO2/FiO2) and

mechanical power. Systematic review and meta-analysis with meta-regression. Med Intensiva (Engl Ed). 2021;45:516–31, http://dx.doi.org/10.1016/j.medine.2021.03.001.
39. Lachmann B. Open up the lung and keep the lung open. Intensive Care Med. 1992;18:319–21, http://dx.doi.org/10.1007/BF01694358.
40. Kneyber MCJ. Positive end-expiratory pressure in the pediatric intensive care unit. Paediatr Respir Rev. 2024;49:5–8, http://dx.doi.org/10.1016/j.prrv.2023.11.003.
41. Khemani RG, Parvathaneni K, Yehya N, Bhalla AK, Thomas NJ, Newth CJL. Positive end-expiratory pressure lower than the ARDS network protocol is associated with higher pediatric acute respiratory distress syndrome mortality. Am J Respir Crit Care Med. 2018;198:77–89, http://dx.doi.org/10.1164/rccm.201707-1404OC.
42. Petrucci N, Iacovelli W. Ventilation with lower tidal volumes versus traditional tidal volumes in adults for acute lung injury and acute respiratory distress syndrome. In: Cochrane database of systematic reviews. Chichester, UK: John Wiley & Sons, Ltd; 2003.
43. Wardi G, Holgren S, Gupta A, Sobel J, Birch A, Pearce A, et al. A review of bicarbonate use in common clinical scenarios. J Emerg Med. 2023;65:e71–80, http://dx.doi.org/10.1016/j.jemermed.2023.04.012.
44. Fernando SM, Qureshi D, Tanuseputro P, Dhanani S, Guerguerian A-M, Shemie SD, et al. Long-term survival and costs following extracorporeal membrane oxygenation in critically ill children—a population-based cohort study. Crit Care. 2020;24:131, http://dx.doi.org/10.1186/s13054-020-02844-3.
45. Papazian L, Aubron C, Brochard L, Chiche J-D, Combes A, Dreyfuss D, et al. Formal guidelines: management of acute respiratory distress syndrome. Ann Intensive Care. 2019;9:69, http://dx.doi.org/10.1186/s13613-019-0540-9.
46. Chilcote D, Sriram A, Slovis J, Morgan RW, Schaubel DE, Connelly J, et al. Venovenous extracorporeal membrane oxygenation initiation for pediatric acute respiratory distress syndrome with cardiovascular instability is associated with an immediate and sustained decrease in vasoactive-inotropic scores. Pediatr Crit Care Med. 2024;25:e41–46, http://dx.doi.org/10.1097/PCC.0000000000003325.
47. Shah N, Li X, Shanmugham P, Fan E, Thiagarajan RR, Venkataraman R, et al. Early changes in arterial partial pressure of carbon dioxide and blood pressure after starting extracorporeal membrane oxygenation in children: extracorporeal life support organization database study of neurologic complications*. Pediatr Crit Care Med. 2023;24:541–50, http://dx.doi.org/10.1097/PCC.0000000000003216.
48. Nakamura Y, Rudolph K, Ricci M, Auslender M, Badheka A. Venoarterial to venovenous extracorporeal life support conversion in pediatric acute respiratory distress syndrome. Perfusion. 2022;37:334–9, http://dx.doi.org/10.1177/02676591211000584.
49. Holton C, Shah S, Miller JO. New right ventricular dysfunction in pediatric acute respiratory distress syndrome on venovenous extracorporeal membrane oxygenation. ASAIO J. 2024;70:994–1000, http://dx.doi.org/10.1097/MAT.0000000000002257.
50. Cui Y, Zhang Y, Dou J, Shi J, Zhao Z, Zhang Z, et al. Venovenous vs. venoarterial extracorporeal membrane oxygenation in infection-associated severe pediatric acute respiratory distress syndrome: a prospective multicenter cohort study. Front Pediatr. 2022;10:832776, http://dx.doi.org/10.3389/fped.2022.832776.
51. Fernandez-Sarmiento J, Perez MC, Bustos JD, Acevedo L, Sarta-Mantilla M, Guijarro J, et al. Association between mechanical ventilation parameters and mortality in children with respiratory failure on ECMO: a systematic review and meta-analysis. Front Pediatr. 2024;12:1302049, http://dx.doi.org/10.3389/fped.2024.1302049.
52. Friedman ML, Abu-Sultaneh S, Slaven JE, Mastropietro CW. Rest ventilator management in children on veno-venous extracorporeal membrane oxygenation. Int J Artif Organs. 2022;45:174–80, http://dx.doi.org/10.1177/0391398821999386.
53. Kneyber MCJ, Cheifetz IM. Mechanical ventilation during pediatric extracorporeal life support. Curr Opin Pediatr. 2023;35:596–602, http://dx.doi.org/10.1097/MOP.0000000000001277.
54. Teijeiro-Paradis R, Ferguson ND. Prone positioning during venovenous ECMO for severe ARDS. JAMA. 2023;330:2341, http://dx.doi.org/10.1001/jama.2023.22456.
55. Rowan CM, Randolph AG, Iyer NP, Korang SK, Kneyber MCJ. Pulmonary specific ancillary treatment for pediatric acute respiratory distress syndrome: from the Second Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med. 2023;24 Supplement 1 2S:S99–111, http://dx.doi.org/10.1097/PCC.0000000000003162.
56. Qin W, Mao L, Shen Y, Zhao L. Prone position in the mechanical ventilation of acute respiratory distress syndrome children: a systematic review and meta-analysis. Front Pediatr. 2024;12:1293453, http://dx.doi.org/10.3389/fped.2024.1293453.
57. Xiang L, Ren H, Wang Y, Wang Z, Frerichs I, Zhao Z. Prone positioning improved ventilation-perfusion matching in severe pediatric acute respiratory distress syndrome. Am J Respir Crit Care Med. 2023;207:e75–76, http://dx.doi.org/10.1164/rccm.202208-1571IM.
58. Bhandari AP, Nnate DA, Vasanthan L, Konstantinidis M, Thompson J. Positioning for acute respiratory distress in hospitalised infants and children. Cochrane Database Syst Rev. 2022;6:CD003645, http://dx.doi.org/10.1002/14651858.CD003645.pub4.
59. Zheng Y-R, Lei Y-Q, Liu J-F, Wu H-L, Xu N, Huang S-T, et al. Effect of high-frequency oscillatory ventilation combined with pulmonary surfactant in the treatment of acute respiratory distress syndrome after cardiac surgery: a prospective randomised controlled trial. Front Cardiovasc Med. 2021;8:675213, http://dx.doi.org/10.3389/fcvm.2021.675213.
60. Curley MAQ, Hibberd PL, Fineman LD, Wypij D, Shih M-C, Thompson JE, et al. Effect of prone positioning on clinical outcomes in children with acute lung injury. JAMA. 2005;294:229, http://dx.doi.org/10.1001/jama.294.2.229.
61. Kneyber MCJ, Cheifetz IM, Asaro LA, Graves TL, Viele K, Natarajan A, et al. Protocol for the Prone and Oscillation Pediatric Clinical Trial (PROSpect). Pediatr Crit Care Med. 2024;25:e385–396, http://dx.doi.org/10.1097/PCC.0000000000003541.
62. Constantin J-M, Grasso S, Chanques G, Aufort S, Futier E, Sebbane M, et al. Lung morphology predicts response to recruitment maneuver in patients with acute respiratory distress syndrome. Crit Care Med. 2010;38:1108–17, http://dx.doi.org/10.1097/CCM.0b013e3181d451ec.
63. Cavalcanti AB, Suzumura ÉA, Laranjeira LN, Paisani D de M, Damiani LP, Guimarães HP, et al. Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome. JAMA. 2017;318:1335, http://dx.doi.org/10.1001/jama.2017.14171.
64. Chidini G, Raimondi F. Lung ultrasound for the sick child: less harm and more information than a radiograph. Eur J Pediatr. 2023;183:1079–89, http://dx.doi.org/10.1007/s00431-023-05377-3.
65. Bobot M, Tonon D, Peres N, Guervilly C, Lefèvre F, Max H, et al. Impact of dexamethasone and inhaled nitric oxide on severe

acute kidney injury in critically ill patients with COVID-19. J Clin Med. 2022;11:6130, http://dx.doi.org/10.3390/jcm11206130.
66. Vuillermoz A, Lefranc M, Prouvez N, Brault C, Zerbib Y, Schmitt M, et al. Modes of administration of nitric oxide devices and ventilators flow-by impact the delivery of predetermined concentrations. Ann Intensive Care. 2024;14:130, http://dx.doi.org/10.1186/s13613-024-01351-w.
67. Berger JT, Maddux AB, Reeder RW, Banks R, Mourani PM, Berg RA, et al. Inhaled nitric oxide use in pediatric hypoxemic respiratory failure*. Pediatr Crit Care Med. 2020;21:708–19, http://dx.doi.org/10.1097/PCC.0000000000002310.
68. Dobyns EL, Cornfield DN, Anas NG, Fortenberry JD, Tasker RC, Lynch A, et al. Multicenter randomized controlled trial of the effects of inhaled nitric oxide therapy on gas exchange in children with acute hypoxemic respiratory failure. J Pediatr. 1999;134:406–12, http://dx.doi.org/10.1016/s0022-3476(99)70196-4.
69. Smith HAB, Besunder JB, Betters KA, Johnson PN, Srinivasan V, Stormorken A, et al. 2022 Society of Critical Care Medicine Clinical Practice Guidelines on prevention and management of pain, agitation, neuromuscular blockade, and delirium in critically ill pediatric patients with consideration of the ICU environment and early mobility. Pediatr Crit Care Med. 2022;23:e74–110, http://dx.doi.org/10.1097/PCC.0000000000002873.
70. Klompas M, Branson R, Cawcutt K, Crist M, Eichenwald EC, Greene LR, 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;43:687–713, http://dx.doi.org/10.1017/ice.2022.88.
71. Blakeman TC, Scott JB, Yoder MA, Capellari E, Strickland SL. AARC clinical practice guidelines: artificial airway suctioning. Respir Care. 2022;67:258–71, http://dx.doi.org/10.4187/respcare.09548.
72. Leow EH, Wong JJ-M, Mok YH, Hornik CP, Ng YH, Lee JH. Fluid overload in children with pediatric acute respiratory distress syndrome: a retrospective cohort study. Pediatr Pulmonol. 2022;57:300–7, http://dx.doi.org/10.1002/ppul.25720.
73. Li Y, Wang J, Bai Z, Chen J, Wang X, Pan J, et al. Early fluid overload is associated with acute kidney injury and PICU mortality in critically ill children. Eur J Pediatr. 2016;175:39–48, http://dx.doi.org/10.1007/s00431-015-2592-7.
74. Lee J, Corl K, Levy MM. Fluid therapy and acute respiratory distress syndrome. Crit Care Clin. 2021;37:867–75, http://dx.doi.org/10.1016/j.ccc.2021.05.012.
75. Valentine SL, Kudchadkar SR, Ward S, Morrow BM, Nadkarni VM, Curley MAQ. Nonpulmonary treatments for pediatric acute respiratory distress syndrome: from the second pediatric acute lung injury consensus conference. Pediatr Crit Care Med. 2023;24 Supplement 1 2S:S45–60, http://dx.doi.org/10.1097/PCC.0000000000003158.
76. Sinha P, Furfaro D, Cummings MJ, Abrams D, Delucchi K, Maddali MV, et al. Latent class analysis reveals COVID-19–related acute respiratory distress syndrome subgroups with differential responses to corticosteroids. Am J Respir Crit Care Med. 2021;204:1274–85, http://dx.doi.org/10.1164/rccm.202105-1302OC.
77. Chang X, Li S, Fu Y, Dang H, Liu C. Safety and efficacy of corticosteroids in ARDS patients: a systematic review and meta-analysis of RCT data. Respir Res. 2022;23:301, http://dx.doi.org/10.1186/s12931-022-02186-4.
78. Barajas-Romero JS, Vásquez-Hoyos P, Pardo R, Jaramillo-Bustamante JC, Grigolli R, Monteverde-Fernández N, et al. Factors associated with prolonged mechanical ventilation in children with pulmonary failure: cohort study from the LARed Network registry. Med Intensiva (Engl Ed). 2024;48:23–36, http://dx.doi.org/10.1016/j.medine.2023.07.001.
79. Loh SW, Gan MY, Wong JJ, Ong C, Mok YH, Lee JH. High burden of acquired morbidity in survivors of pediatric acute respiratory distress syndrome. Pediatr Pulmonol. 2021;56:2769–75, http://dx.doi.org/10.1002/ppul.25520.
80. Medina Villanueva A, Modesto i Alapónt V, Reyes-Dominguez, López Fernández Y. Ventilación mecánica en el síndrome de distrés respiratorio agudo. Capítulo 32. In: Medina Villanueva A, editor. Manual de Ventilación Mecánica Pediátrica y Neonatal. iBook; 2022. ISBN 978-84-123534-2-3.