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Management of paediatric acute respiratory distress syndrome

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Learning objectives

By reading this article, you should be able to:

- Describe pulmonary mechanics and the difference between adults and children.
- Illustrate the development of lung injury and the impact on normal physiology.
- Familiarise yourself with the Pediatric Acute Lung Injury Consensus Conference (PALICC), paediatric-specific definition of ARDS.
- Be aware of and understand the additional ventilatory and non-ventilatory management strategies available for paediatric patients.
- Explain high-frequency oscillation ventilation (HFOV) and the basics of its use.

Key points

- The Pediatric Acute Lung Injury Consensus Conference (PALICC) developed a paediatric-specific definition of ARDS, introducing the concept of pulmonary parenchymal disease rather than bilateral infiltrates suggested in the more adult focused Berlin definition.[1]
- Pediatric Acute Lung Injury Consensus Conference suggested the use of pulse oximetry to stratify impaired oxygenation using the oxygenation index/oxygenation saturation index rather than the P/F ratio.
- High-frequency oscillatory ventilation is used in children to treat refractory hypoxaemia when conventional mechanical ventilation has failed.
- The mechanisms of gas exchange during HFOV are distinct from those of conventional ventilation and therefore the initiation, monitoring, titration and weaning processes differ.
- There are few robust clinical trials to guide practice; therefore, the use of HFOV in PARDS is generally based on the experience of the institution.

Paediatric acute respiratory distress syndrome (PARDS) is a significant cause of mortality and morbidity in children who frequently need admission to PICU with few effective therapies.[2] Ashbaugh and colleagues[2] first reported the pathophysiological abnormalities found in acute respiratory distress syndrome (ARDS) in 1967. In 1994 the American–European Consensus Conference (AECC) defined ARDS as 'wide-spread bilateral pulmonary infiltrates on CXR; associated hypoxaemia (PF <200) and the absence of elevated pulmonary capillary wedge pressure (PCWP) or other evidence of left atrial hypertension'.[3] Seventeen years later, a second consensus conference published the Berlin definition in which the acute lung injury category was removed and instead, a grading of ARDS severity was described, established by the level of impaired oxygenation, with a minimum of 5 cm H_2O PEEP applied.[4] Furthermore, as a result of the infrequent use of pulmonary artery catheters, determining the presence of cardiac failure became more subjective.[4] Both the AECC and Berlin ARDS[5]

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definitions focused on adult lung injury and had significant limitations when applied to children.

These concerns prompted the organisation of the Pediatric Acute Lung Injury Consensus Conference (PALICC) in 2012, and the PALICC definition was published in 2015.[1] The main differences between the PALICC and Berlin definitions are the PALICC concept of pulmonary parenchymal disease rather than bilateral infiltrates, and the use of pulse oximetry with impaired oxygenation stratified using the oxygenation index/oxygenation saturation index rather than P/F ratio (Table 1).

Differences between adult and paediatric anatomy and physiology pertinent to PARDS

The limitations of adult-based definitions and management strategies for ARDS are highlighted when one considers the anatomical and physiological differences between adults and children.

The diameter of the paediatric airway is smaller and more compliant than the adult airway and therefore more predisposed to obstruction. There is a greater increase in airway resistance and work of breathing with a small reduction in airway radius (by the Hagen–Poiseuille formula, resistance is inversely proportional to the fourth power of the radius). As a result, minor obstruction caused by mucous, bronchospasm or oedema has a much greater impact on ventilation pressures leading to an increased risk of barotrauma and volutrauma as a result of increased pressure and volume, respectively.

A barrel-shaped chest with horizontal ribs prevents the 'bucket-handle' movement, limiting an increase in tidal volume. Ventilation is primarily diaphragmatic. An increase in intra-abdominal contents therefore causes diaphragmatic splinting and impairs ventilation. The limited ability to increase tidal volume means that minute ventilation largely depends on the ventilatory frequency. Furthermore, neonates and infants have a lower percentage of type 1 muscle fibres in the diaphragm which is therefore more prone to fatigue.

Work of respiration is approximately 15% of oxygen consumption and paediatric patients have limited respiratory reserve; therefore, increases in work of breathing and periods of apnoea are poorly tolerated.

The chest wall is notably more compliant than that of the adult resulting in a low functional residual capacity (FRC). Furthermore, the closing volume is larger than the FRC until children are approximately 6–8 yr of age; consequently, there is a propensity for atelectasis and airway closure at end expiration.

During tracheal intubation and ventilatory support, neonates and infants benefit from high ventilatory frequencies and PEEP in addition to intermittent positive pressure ventilation (IPPV). In the same way, during spontaneous ventilation, the application of continuous positive airway pressure (CPAP) may improve oxygenation and decrease the work of breathing. The metabolic requirements and oxygen

Table 1 Comparison of the PALICC definition of paediatric ARDS with the Berlin definition. *For non-invasive mechanical ventilation, there is no severity stratification. The oxygenation criteria with full face-mask bilevel ventilation or CPAP ≥5 cm H_2O is P/F ratio ≤39.9 kPa.[1] †Oxygenation index (OI)=(F_{IO_2} × mean airway pressure × 100)/Pa_{O_2}. ‡Oxygenation saturation index (OSI)=(F_{IO_2} × mean airway pressure × 100)/Sp_{O_2}. ARDS, acute respiratory distress syndrome; CPAP, continuous positive airway pressure; ECHO, Echocardiogram, PALICC, Pediatric Acute Lung Injury Consensus Conference.

	PALICC definition of PARDS[1]	Berlin definition of ARDS[5]
Age	Exclude hypoxaemia secondary to perinatal-related lung disease.	–
Timing	Within 7 days of known clinical insult.	Within 1 week of known clinical insult or new /worsening respiratory symptoms.
Chest imaging	New infiltrate(s) consistent with pulmonary parenchymal disease are necessary.	Bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules.
Origin of oedema	Respiratory failure and new chest imaging not explained by acute left ventricular failure or fluid overload.	Respiratory failure not fully explained by cardiac failure of fluid overload. Echocardiogram required to exclude hydrostatic oedema if no risk factor present.
Oxygenation*	Use of OI† or OSI‡ to stratify severity during invasive mechanical ventilation.	Use of PaO_2/FiO_2 (P/F ratio) to stratify severity.
Mild	4 ≤ OI < 8 5 ≤ OSI < 7.5	26.6 kPa < P/F ratio ≤ 39.9 kPa with PEEP/CPAP ≥ 5 cm H_2O
Moderate	8 ≤ OI <16 7.5 ≤ OSI 12.3	13.3 kPa < P/F ratio ≤ 26.6 kPa with PEEP/CPAP ≥ 5 cm H_2O
Severe	OI ≥ 16 OSI ≥ 12.3	P/F ratio ≤ 13.3 kPa with PEEP/CPAP ≥ 5 cm H_2O
Special considerations[1]		
Cyanotic heart disease	As per PALICC definition above but 'deterioration in oxygenation not explained by underlying cardiac disease'.	
Chronic lung disease	As per PALICC definition above with 'chest imaging changes consistent with new infiltrate and ac acute deterioration in oxygenation from baseline'.	
Left ventricular dysfunction	As per PALICC definition above with 'acute deterioration in oxygenation not explained by left ventricular dysfunction'.	

consumption in children is high and almost twice that of adults at birth. This increases the risk of hypoxia with subsequent anaerobic metabolism and lactate production.

Paediatric patients have a propensity for hypoxia, and when one considers the pathophysiology of PARDS it becomes clear why it has such a significant impact and mortality.

Pathophysiology

The integrity of the alveolar–epithelial and capillary–endothelial barrier is key to maintain gas exchange and lung defence. The impact of PARDS lies in its ability to cause a disruption of this integrity, leading to altered permeability of the alveolar–capillary barrier.[6] The mechanism of this disruption may occur at the level of the alveolar epithelium (e.g. in pneumonia or inhaled toxins) or at the level of the capillary endothelium secondary to systemic inflammation (e.g. in sepsis or acute pancreatitis). The pathological processes involved in ARDS follow three stages. These are the exudative, proliferative and fibrotic stages. When the alveolar endothelial barrier is disrupted, protein-rich fluid is allowed to accumulate in the alveoli. Inflammation is dysregulated, and there is activation of leucocytes, platelets and coagulation with associated damage to the lung epithelium and vascular endothelium.[6] This is accompanied by suppression of fibrinolysis and loss of surfactant. The clinical consequence is a restrictive lung disease pattern secondary to changes in the alveoli, hypoxia, decreased FRC, increased physiological dead space and decreased lung compliance.[6] Recovery and resolution of ARDS involves repair of the epithelium and endothelium which may result in fibrosis. Resolution of the inflammation may take several weeks.

It is important to note that although paediatric data do reveal similarities in the pathophysiological processes of adult ARDS and PARDS, the paucity of paediatric studies becomes an issue when one considers that the lungs and immune system of children are still developing. The pathophysiology of PARDS may therefore differ from that of adults, in particular, the degree and response to lung injury.[6]

Aetiology

The major causes of paediatric ARDS are[7]:

(i) Pneumonia or lower respiratory tract infection (67%)
(ii) Sepsis (16%)
(iii) Aspiration (8%)
(iv) Trauma (4.1%)
(v) Drowning (<1%)
(vi) Non-septic shock (1%)

The highest mortality is seen in victims of drowning (67%), non-septic shock (60%) and sepsis (30%), whereas mortality associated with pneumonia or lower respiratory tract infection was 12%.

Epidemiology

The epidemiology and incidence of PARDS was reported by PARDS incidence and epidemiology (PARDIE), an international observational study carried out between May 2016 and June 2017, which recruited patients from 145 paediatric ICUs across 27 countries. Before this study, little was known about the international epidemiology of PARDS.[7] The researchers found the prevalence of PARDS to be 3.2% and mortality as high as 17%. The PARDIE study also compared both PALICC and Berlin definitions and found that the PALICC definition not only identified PARDS in more children than the Berlin definition, but also found that the PALICC PARDS severity groupings improved the mortality risk stratification – more so when applied 6 h after the diagnosis of PARDS.[7] A further meta-analysis by Wong and colleagues[8] in 2017 found the pooled mortality to be approximately 24% with a decreasing trend over the past 3 yr.

Management strategies of PARDS

Ventilatory strategies and evidence

Mechanical ventilation in patients with PARDS is challenging as ventilation perpetuates lung injury, contributing to both the morbidity and mortality of PARDS. Early recognition and implementation of both ventilatory and non-ventilatory strategies is key to improving survival and is focused on the use of lung protective ventilation.

Mode of ventilation

There is currently no outcome data available to show superiority of either the controlled or assisted mode during conventional mechanical ventilation in PARDS, and further clinical trials are required before a recommendation can be made.[1]

Tidal volumes, peak inspiratory pressure and plateau pressure

Pediatric Acute Lung Injury Consensus Conference recommends tidal volumes of between 5 and 8 ml kg^{-1} predicted body weight.[1] However, this is recommended for patients with better preserved respiratory compliance. Disease severity should be taken into consideration with lower tidal volumes (3–6 ml kg^{-1} predicted body weight) used in patients with poor respiratory compliance.[1] Lower tidal volumes (6 ml kg^{-1} predicted body weight) have been associated with a decreased mortality and more ventilator-free days in adult studies.[9]

The relationship between mortality and peak inspiratory pressure (PIP) is linear. It is recommended that plateau pressures are limited to $\leq$28 cm H_2O. In patients with decreased chest wall compliance, a higher plateau pressure (29–32 cm H_2O) may be acceptable.[1] It is important to note that as paediatric tracheal tubes may be uncuffed with variable inspiratory flow ventilation used, PIP is sometimes therefore substituted for plateau pressure.[10]

Positive end-expiratory pressure

There are few data on the optimal levels of PEEP in paediatrics. However, meta-analyses looking at the use of PEEP in adults with ARDS found that higher levels of PEEP used as part of lung-protective ventilation in adult patients with ARDS and a P/F ratio $\leq$26.6 kPa resulted in lower hospital mortality.[11] The PALICC recommendation is therefore PEEP between 10 and 15 cm H_2O, which should be titrated to oxygenation and haemodynamic response in severe PARDS. If PEEP >15 cm H_2O is required, one should still be mindful of limiting the plateau pressure.[1]

Recruitment manoeuvres

Generally, the response to recruitment manoeuvres in those with reduced lung compliance is poorer than those with reduced chest wall compliance.[10] However, if the respiratory pathology is related to alveolar collapse or oedema, the response to recruitment manoeuvres is better despite the reduction in lung compliance.[10]

Although there is a lack of evidence, the PALICC recommendation in severe oxygenation failure is careful recruitment manoeuvres by slow stepwise increase and decrease of PEEP.[1] Sustained inflation is not recommended as it may lead to overdistension by preferential delivery of pressure to the alveoli that are already open.[12]

Gas exchange targets

There should be a risk–benefit balance between oxygenation/ventilation targets and lung injury.

In adult patients with ARDS, increased oxygenation does not correlate with improved outcomes.[9] Furthermore, a low tidal volume (6 ml kg^{-1}) showed improved survival despite lower average saturations than those with a high tidal volume (12 ml kg^{-1}).[9]

As a result, permissive hypoxia is recommended by PALICC; therefore, saturations between 92% and 97% in mild PARDS with a PEEP <10 cm H_2O and 88–92% in severe PARDS with an optimised PEEP >10 cm H_2O may be acceptable.[1] Oxy-PICU is a randomised multicentre trial currently recruiting critically ill children who are mechanically ventilated to receive either conservative or liberal oxygenation targets. It aims to review whether the harm of intervention increasing Spo_2 to >94% may exceed benefits.[4]

Permissive hypercapnoea with a pH between 7.15 and 7.3 is also recommended by PALICC; however, patients with 'intracranial hypertension, severe pulmonary hypertension, selected congenital heart disease, haemodynamic instability and significant ventricular dysfunction should be excluded'.[1]

High-frequency oscillatory ventilation

High-frequency oscillatory ventilation (HFOV) is used to treat refractory hypoxaemia when conventional mechanical ventilation has failed.

The benefit is thought to be in its ability to prevent atelectrauma and volutrauma by using higher mean airway pressures (essentially a high CPAP) while delivering minimal tidal volumes (1–3 ml kg^{-1}, approximately anatomical dead space) at supranormal rates (3–20 Hz, 180–1200 bpm), minimising ventilator-induced lung injury and improving gas exchange.[13]

Gas exchange

Gas exchange during HFOV is achieved through a number of mechanisms.[13]

Bulk flow is direct ventilation seen in the more proximal alveolar units with short path lengths.

Taylor dispersion, seen in the large airways. In the presence of laminar flow, the centre of the gas column travels faster than the outer area (parabolic surface), which allows greater longitudinal mixing and diffusion downstream. Turbulence occurs when a bifurcation is reached, causing further dispersion of gas molecules and therefore further gas exchange.

Pendelluft mixing, seen in small peripheral airways and alveoli. There is regional mixing as gas equilibrates between compliant and non-compliant alveolar units. Gas moves from the compliant alveolar unit to the non-compliant alveolar unit at end expiration because the compliant area continues to empty when the non-compliant area is already empty. The opposite occurs at end inspiration as the non-compliant alveolar unit is already full when the compliant alveolar unit continues to fill. There is therefore a pendulum-like movement of air between neighbouring alveoli leading to collateral ventilation.

Molecular diffusion involves passive diffusion of gas through the alveolar capillary membrane.

Cardiogenic mixing involving agitation of surrounding lung tissue with molecular diffusion.

The OSCILLATE (Oscillation for Acute Respiratory Distress Syndrome Treated Early) and OSCAR (High Frequency Oscillation in ARDS) were two RCTs using HFOV.[14,15] The OSCILLATE trial found a higher mortality and a greater use of vasopressors, sedation and neuromuscular blockers in the HFOV group.[14] However, 50% of patients in this trial had sepsis; therefore, the use of high mean airway pressures may have further compromised the haemodynamic instability seen in sepsis, which may account for the increased use of vasopressors and increased mortality.[10] The OSCAR trial found no significant difference in mortality between the HFOV and conventional mechanical ventilation groups.[15] It is, however, important to note that in the OSCAR trial, although the study did involve training, most participating centres were not experienced with the use of HFOV.[10]

The Prone and Oscillation Pediatric Clinical Trial (PROSpect) is a randomised controlled trial, currently recruiting paediatric patients with moderate to severe PARDS (OI > 12) who are randomised to test the hypothesis that 'prone versus supine positioning and HFOV versus conventional mechanical ventilation (CMV) will result in a 2-day improvement in ventilator-free days'.[16] For now, there is still a lack of evidence for the use of HFOV in PARDS and until there are robust clinical trials to guide our practice, the use of HFOV in PARDS is generally based on the experience of the institution.

When to consider HFOV in PARDS

Pediatric Acute Lung Injury Consensus Conference recommends that HFOV be considered in patients with moderate to severe PARDS where plateau pressures are ≥28 cm H_2O in the absence of reduced chest wall compliance.[1]

Initiating HFOV

Practical HFOV use and management is often based on institutional experience and varies from centre to centre. Practice at our institution is outlined below.

High-frequency oscillation ventilation should be considered when the PIP >30 cm H_2O, F_{IO_2} >0.6, MAP ≥16 H_2O or with an OI >15 without improvement on conventional ventilation.[17]

(i) Sensormedics A for neonates and children up to 30 kg
(ii) Sensormedics B for all other children and adults
(iii) Before initiating HFOV, the blood pressure and perfusion must be optimised
(iv) Neuromuscular block is usually required

Initial settings

(i) Mean airway pressure is set at 2–4 cm H_2O above the last MAP during conventional ventilation.

(ii) F_{IO_2} is set to 1.0 to start and can be weaned as able.
(iii) Frequency (1 Hz=60 bpm) is set by age: preterm 10–13 Hz; term 8–10 Hz; children 6–8 Hz.
(iv) Amplitude Delta P (ΔP) is the driving pressure providing gas movement represented by oscillations which should be visible from chest to mid-thigh. This depends on the patient size and pulmonary compliance. It is usually started at twice the set MAP (about 20–25 cm H_2O), then increased by 3–5 cm H_2O until the chest wall oscillations are visible.
(v) The inspiratory:expiratory (I:E) ratio is set at 1:3 (33%).

Monitoring during HFOV

(i) A chest X-ray should be performed soon after initiating HFOV,[13] then monitor for hyperinflation.
(ii) Blood gases should be performed half an hour after initiation and after any change to settings.
(iii) The P/F ratio and oxygenation index should be calculated.

Troubleshooting during HFOV

(i) If the patient is hypoxic, consider increasing the F_{IO_2}. If there is no improvement, adjust the MAP by increments of 1 cm H_2O at a time and if the hypoxia persists then consider getting a chest X-ray.
(ii) If hypercarbia is the problem, then assess the oscillation of the chest. If this is optimal, then exclude tracheal tube obstruction and consider suction. If there is still no resolution, adjust the amplitude (ΔP) in increments of 2–4 cm H_2O and consider decreasing the frequency.
(iii) When restarting HFOV, start at the lowest frequency and highest cycle volume.
(iv) If the patient is hypotensive, assess the fluid status, consider a fluid bolus or inotropic support, also and look for hyper-expansion and if this is the case then decrease the MAP by 1–2 cm H_2O at a time until it is optimised.
(v) If there is no improvement in the patient's ventilation/oxygenation, consider neuromuscular blocking agents if not already commenced, then increase the MAP by 1–2 cm H_2O.
(vi) If there is still no improvement, then the ventilation strategy needs to be re-evaluated as conventional ventilation may be a more suitable option.

Weaning from HFOV

- Reduce F_{IO_2} to <0.4 before weaning MAP (except when over inflation is evident).
- Reduce MAP in 1–2 cm H_2O decrements 1–2 hourly or as tolerated. Wean to conventional ventilation when MAP <16–15 cm H_2O.
- Wean the ΔP as MAP is decreased.

Once MAP is around 15 cm H_2O, change to conventional ventilation.

Non-ventilatory strategies and evidence

Corticosteroids

It is hypothesised that when corticosteroids are given early in the course of ARDS, there may be a decrease in subsequent fibrotic tissue formation.

A meta-analysis looking at studies using low-to-moderate dose steroids for a prolonged period found glucocorticoid therapy to be safe, decreasing the time to tracheal extubation, duration of hospitalisation and mortality also increasing ventilator-free days, and decreasing ICU stay, and hospitalisation. Recent adult intensive care guidelines recommend giving methylprednisolone in patients with early moderate-to-severe (1 mg kg^{-1} day^{-1}) and late persistent (2 mg kg^{-1} day^{-1}) ARDS.[18]

An RCT looking at patients with PARDS who received a low-dose methylprednisolone infusion found no difference in mortality, ICU admission, duration of mechanical ventilation and hospital stay.[19] However, this study was limited by its small sample size (n=17 for steroid group and n=18 for placebo group).[19]

Observational paediatric data show a longer duration of mechanical ventilation with greater than 24 h of corticosteroid use.[20] However, a later, retrospective, observational study looked at the change in oxygen saturation index (OSI), after low-dose methylprednisolone in patients with PARDS, to identify the proportion of children demonstrating a response with or without a reduction in the mean PICU OSI, and the possible characteristics that predict a response to therapy. They found that the mean OSI of the cohort increased until the day of starting steroid therapy, then improved thereafter. Results showed that 59% of patients demonstrated a response to steroids, and baseline characteristics were similar between responders and non-responders, whereas the survival to PICU discharge was significantly higher in 'responders' (74% *vs* 41%). On multivariable analysis using likely confounders, response to steroid was an independent predictor of survival to PICU discharge (P=0.002). Non-responders died earlier after steroids than responders (P=0.003).[21]

Pediatric Acute Lung Injury Consensus Conference does not currently recommend the use of corticosteroids as routine therapy in PARDS as there are insufficient paediatric data available.[1]

Inhaled nitric oxide

Inhaled nitric oxide (iNO) is a short-acting selective pulmonary vasodilator that acts via cyclic 3,5-guanosine monophosphate (cGMP)-mediated opening of calcium-dependent K^+ channels. It is thought to improve oxygenation by predominantly causing vasodilation in the well-ventilated regions of the lung directing blood away from poorly ventilated parts, leading to a reduction in the ventilation/perfusion mismatch.[10] It is particularly effective in conditions in which increased pulmonary pressure is a major element of the disease process, for example neonatal pulmonary hypertension and congenital heart disease.

Despite improved short-term oxygenation, RCTs in children with PARDS show no benefit.[22]

Pediatric Acute Lung Injury Consensus Conference does not recommend the routine use of inhaled nitric oxide in PARDS except in patients with confirmed pulmonary hypertension or severe right ventricular dysfunction and as a bridge to extracorporeal membrane oxygenation (ECMO) in patients with severe PARDS.[1]

Prone positioning

The prone position results in improved oxygenation by decreasing the ventral–dorsal transpulmonary pressure difference, decreasing lung compression by the heart and

diaphragm and improving lung perfusion in dependant portions to match ventilation.

The adult Proning in Severe ARDS (PROSEVA) trial showed a 50% reduction in mortality in patients with severe ARDS on early application of prolonged prone-positioning sessions.[23] In contrast, a paediatric RCT showed no difference in outcome although 90% of proned patients showed an improvement in oxygenation.[24] It is important to note that the paediatric study enrolled patients with mild to severe ARDS in contrast to the adult study, which only included patients with severe ARDS.[10] Prone positioning in critically ill infants and children is, however, found to be safe.[25]

Pediatric Acute Lung Injury Consensus Conference recommends considering prone positioning in severe ARDS but cannot recommend its use as routine therapy.[1] The PROSpect trial looking into prone positioning and HFOV in severe PARDS is still ongoing.[16]

Exogenous surfactant

No outcome benefit is seen with exogenous surfactant in both adult and paediatric studies.[10] Although PALICC cannot recommend the routine use of exogenous surfactant in PARDS, it does recommend that further studies be conducted, focusing on patient groups that may be likely to benefit from its use.

Neuromuscular block

Neuromuscular block in the first 48 h of ARDS in adults with severe disease showed improved survival and ventilator-free days.[26] The PETAL (Prevention and Early Treatment of Acute Lung Injury) network trial, however, found no significant difference in 90-day mortality between adult patients with moderate-to-severe ARDS who received, early, continuous cisatracurium infusions and those who were treated without routine neuromuscular block.[27] A paediatric observational study showed improved oxygenation index in patients with hypoxic respiratory failure who received neuromuscular block, but longer-term outcomes and survival were not assessed.[10] The recommendation made by PALICC is to consider neuromuscular block if adequate mechanical ventilation cannot be achieved by sedation alone.[1]

Fluids

There are currently no RCTs conducted on fluid management in PARDS. A *post hoc* analysis looked at 320 paediatric patients with acute lung injury and found that a positive fluid balance, with or without multi-organ failure, was associated with increased mortality and duration of mechanical ventilation irrespective of the degree of oxygen impairment.[28] The Fluid and Catheter Treatment Trial (FACTT), a randomised, multicentred trial compared controlled (cumulative fluid balance of −136 [491] ml in the first 7 days) *vs* liberal (cumulative fluid balance 6992 [502] ml in the first 7 days) fluid management in adults with ARDS.[29] This study favoured a controlled approach which improved pulmonary function, and reducing the duration of mechanical ventilation and intensive care stay without increasing non-pulmonary organ failure.[29] However, there was no mortality difference.[29]

Pediatric Acute Lung Injury Consensus Conference recommends goal-directed fluid management, ensuring adequate intravascular volume while avoiding a positive fluid balance after, initial fluid resuscitation and stabilisation.[1]

Extracorporeal membrane oxygenation

There is limited evidence for the use of ECMO in PARDS; however, ECMO use in children has increased. The Extracorporeal Life Support Organisation (ELSO) found that the overall 'survival to hospital discharge' rate for children who received ECMO for refractory respiratory failure in 2019 was 60%. Meanwhile, PALICC recommends that ECMO be considered in patients with severe PARDS in which lung protective ventilatory strategies result in inadequate gas exchange, and the respiratory failure is thought to be reversible. Box 1 shows suggested indications for paediatric respiratory ECMO.

Box 1
Suggested indications for paediatric respiratory ECMO.[30]

- Inadequate gas exchange at risk of ventilator-induced lung injury
  - Sustained P/F ratios <60–80 or OI >40
  - Failure of mechanical ventilation despite other rescue therapy (HFOV/iNO/prone positioning)
  - MAP>20–25 cm H_2O on conventional ventilation or MAP >30 cm H_2O on HFOV
- Hypercapnoeic respiratory failure(pH <7.1) despite appropriate ventilator and patient management

Other criteria to consider:

- Weight >2.0 kg
- Newborn >34 weeks' gestation
- Disease is thought to be reversible (unless bridge-to-transplant)
- No contraindication to systemic anticoagulation (intracranial haemorrhage)
- No lethal congenital abnormalities
- No irreversible organ dysfunction including neurological injury
- No major immunodeficiency
- Rate of deterioration and how quickly ECMO can be initiated

These are suggested indications and not an exhaustive list. Referral to an ECMO centre may often be required earlier in the disease process.

Conclusions

The lack of high-quality studies to support evidence-based management in PARDS has led to variability in practice and, although outcomes have improved, the morbidity and mortality remains significant. Pediatric Acute Lung Injury Consensus Conference has provided us with a definition and recommendations to guide paediatric practice but the management of PARDS and in particular the practice around adjunctive therapies would benefit from more high-quality research.

Declaration of interests

The authors declare that they have no conflicts of interest.

MCQs

The associated MCQs (to support CME/CPD activity) will be accessible at www.bjaed.org/cme/home by subscribers to *BJA Education*.

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