Monitoring of Children With Pediatric Acute Respiratory Distress Syndrome: Proceedings From the Pediatric Acute Lung Injury Consensus Conference

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The Pediatric Acute Lung Injury Consensus Conference Group is listed in **Appendix 1**.

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Objective: To critically review the potential role of monitoring technologies in the management of pediatric acute respiratory distress syndrome, and specifically regarding monitoring of the general condition, respiratory system mechanics, severity scoring parameters, imaging, hemodynamic status, and specific weaning considerations.

Design: Consensus conference of experts in pediatric acute lung injury.

Methods: A panel of 27 experts met over the course of 2 years to develop a taxonomy to define pediatric acute respiratory distress syndrome and to make recommendations regarding treatment and research priorities. The monitoring subgroup comprised two experts. When published data were lacking a modified Delphi approach, emphasizing strong professional agreement was used.

Results: The Pediatric Acute Lung Injury Consensus Conference experts developed and voted on a total of 151 recommendations addressing the topics related to pediatric acute respiratory distress syndrome, 21 of which related to monitoring of a child with pediatric acute respiratory distress syndrome. All 21 recommendations had agreement, with 19 (90%) reaching strong agreement.

Conclusions: The Consensus Conference developed pediatric-specific recommendations related to monitoring children with pediatric acute respiratory distress syndrome. These include interpreting monitored values such as tidal volume using predicted body weight, monitoring tidal volume at the end of the endotracheal tube in small children, and continuous monitoring of exhaled carbon dioxide in intubated children with pediatric acute respiratory distress syndrome, among others. These recommendations for monitoring in pediatric acute respiratory distress syndrome

are intended to promote optimization and consistency of care for children with pediatric acute respiratory distress syndrome and identify areas of uncertainty requiring further investigation. (*Pediatr Crit Care Med* 2015; 16:S86–S101)

Key Words: acute respiratory distress syndrome; children; mechanical ventilation monitoring; pediatric intensive care unit; respiratory mechanics

Close monitoring of physiological parameters is one of the core functions of the pediatric ICU (PICU) environment. Many conditions that cause a pediatric patient to be admitted into PICU are associated with a risk of pediatric acute respiratory distress syndrome (PARDS). Such conditions and the associated need for assisted ventilation are an introduction to equipment with an almost endless capacity to produce measurements of a range of physiological parameters. The objective of this article is to review critically the potential role of these technologies in the management of PARDS, and specifically regarding monitoring of the general condition, respiratory system mechanics, severity scoring parameters, imaging, hemodynamic status, and specific weaning considerations. Much of the ventilation and monitoring equipment used in the PICU environment is derived from adult equipment. The relevance and the use of measuring many of these same parameters in pediatric patients remain unproven. The range of monitoring and the relative complexity and invasiveness thereof increase with the severity of the patient's clinical condition. The challenge for pediatric intensivists is to decide whether monitoring various physiological parameters can be helpful to guide ventilation strategies to minimize the risk of lung injury and improve patient outcomes. A better understanding of each technology benefit/risk balance should help the clinicians in this decision, aiming to raise our practice above "routine monitoring." However, the deficits in our scientific knowledge underline the importance of the collaborative efforts to improving the evidence-base of PARDS management, and in particular of monitoring in PICU.

In this article, we report the rationale of the recommendations on monitoring of the pediatric international consensus conference on PARDS. **Table 1** describes the parameters where there was a strong level of agreement in regard to monitoring in children with PARDS. **Table 2** summarizes the main characteristics and potential of other parameters in which indications to monitor requires more validation.

GENERAL MONITORING

Recommendations

6.1.1 We recommend that all children with or at risk of PARDS should receive the minimum clinical monitoring of respiratory frequency, heart rate, continuous pulse oximetry, and noninvasive blood pressure. *Strong agreement*

6.1.2 We recommend that specific alarms should be available when the monitored parameters are outside predefined ranges. *Strong agreement*

6.1.3 We recommend that some monitored values (eg, tidal volume and compliance of the respiratory system) should be interpreted after standardization to body weight. Hence, accurate weight is critical. Predicted body weight should be used, based on calculation from gender and from height or length or from ulna length. *Strong agreement*

Rationale

PARDS constitutes a severe disease, with a significant risk of complications and mortality. In that context, children with PARDS should at least benefit from the minimal monitoring routinely used in PICUs, including continuous monitoring of cardiac and respiratory rates, pulse oximetry, and blood pressure. The aim of the monitoring of these variables and the various variables discussed below is to diagnose PARDS, assess its severity, and detect any change in the disease severity or any complications. Therefore, all monitored data should be related to specific alarms, the triggers of which being adjusted depending on age, severity, and stage of the disease.

Key physiologic and developmental considerations of children compared with adults make assessments of the impact of tidal volume on outcome challenging. Adult practice is to calculate tidal volume from predicted body weight for age, height, and gender using a set of readily available tables. The rationale is that although obesity is a major problem in adults, it is unlikely that the lungs are obese (ie, larger) and, therefore, the predicted body weight should be the one used for calculation of tidal volume. Although pediatric practice is not entirely clear, actual body weight is most commonly used to calculate tidal volume. Obesity is also a problem in pediatric practice, but so is failure to thrive with low weight for age and height. In addition, contractures and spinal deformities are common, making direct measurement of length or its usual surrogate, arm span, irrelevant. Formulae are now available using ulna length to determine height to predict body weight from birth to 19½ years (1, 2). From growth grids, this height is used to find the appropriate body weight to which tidal volume can be targeted. Nonetheless, it is not known whether the lungs fail to grow appropriately when a child fails to thrive. To approximate the "correct" tidal volume for mechanical ventilation, the best compromise at this time may be to use the actual body weight if the child's weight is less than or equal to the 50th percentile and ideal body weight (IBW) (ie, predicted from height or ulna length) if above the 50th percentile.

RESPIRATORY SYSTEM MECHANICS

Recommendations

6.2.1 We recommend that, during invasive ventilation in children with PARDS, the exhaled tidal volume should be continuously monitored to prevent injurious ventilation. *Strong agreement*

6.2.2 We recommend that monitoring of ventilatory inspiratory pressure is important to prevent ventilator-induced lung injury. It should be based on peak pressure in pressure-regulated modes, and plateau pressure during ventilation in volume-control modes. It should be interpreted with caution

TABLE 1. Parameters That Should Be Monitored in the Management of a Children With Acute Respiratory Distress Syndrome (Strong Agreement)

Parameter	Clinical Information	Phase of the Disease	Continuous or Intermittent Monitoring	Monitor and Equipment	Risk
Routine clinical monitoring in pediatric ICU, including at least respiratory frequency, heart rate, continuous pulse oximetry, and noninvasive blood pressure	Rapid detection of status changes	All	Continuous	Bedside monitor	None
Tidal volume (exhaled) Peak pressure (in pressure-regulated mode) Plateau pressure (in volume-control mode)	Prevention of ventilator-induced lung injury Accuracy of the support	All	Continuous	Ventilator or stand-alone respiratory monitor	None
Flow/time curve Pressure/time curve Volume/time curve	Accuracy of respiratory timings Expiratory limitation Asynchrony detection	Acute	Continuous	Ventilator	None
FIO_2, SpO_2, positive end-expiratory pressure, mean airway pressure	Acute respiratory distress syndrome detection Severity assessment Management of oxygenation failure	All	Continuous	Ventilator, monitor	None
Continuous CO_2 monitoring, with either end-tidal CO_2, volumetric capnography, and/or transcutaneous CO_2 monitoring	Accuracy of the support	All	Continuous	Ventilator, monitor, or specific analyzer	None
Arterial blood gas, capillary blood gas	Severity Accuracy of support	All	Intermittent	Arterial line or puncture Laboratory	Minimal
Standard chest x-ray	Diagnosis Severity assessment Barotrauma detection Equipment position	Acute	Intermittent	Portable x-ray	Minimal
Hemodynamic evaluation (see the different options in Table 2)	To guide fluid strategy, Right and left cardiac function Pulmonary hypertension To assess oxygen transport	Acute	Intermittent	Depends on the method (Table 2)	Depends on the method (Table 2)
Spontaneous breathing test	Extubation readiness	Weaning	Intermittent	Ventilator, clinical data	Minimal

in patients with suspected abnormal chest wall compliance or with spontaneous breathing. *Strong agreement*

6.2.3 We recommend the monitoring of flow-time and pressure-time curves to assess the accuracy of respiratory timings and to detect expiratory flow limitation or patient-ventilator asynchrony. *Strong agreement*

6.2.4 We recommend that in infants and smaller children, the exhaled tidal volumes should be monitored at the end of the endotracheal tube (ETT) and/or with appropriate compensation for circuit compliance. *Strong agreement*

6.2.5 There is insufficient evidence to recommend the systematic monitoring of the following parameters of respiratory system mechanics: flow-volume loop, static pressure-volume loop, dynamic pressure-volume loop, dynamic compliance and resistance, stress index, intrinsic positive end-expiratory pressure (PEEP), esophageal manometry and transpulmonary pressure, work of breathing, corrected minute ventilation ($\dot{V}E_{CORR}$), functional residual capacity (FRC), deadspace/tidal volume ratio, assessment of respiratory muscle activity using airway occlusion pressure ($P_{0.1}$), esophageal pressure-rate

product, electrical activity of diaphragm (EAdi), ultrasonography of the diaphragm, or thoracoabdominal asynchrony (TAA) quantification by respiratory inductance plethysmography. *Weak agreement (92% agreement)*

Rationale

Respiratory System Variables Derived From Measurement in Airway Circuit. During mechanical ventilation in PARDS, bedside measurement of pulmonary mechanics provides important information related to the status of the disease and the impact of mechanical ventilation. A retrospective study of 468 ventilated infants suggested that regular pulmonary function testing may limit ventilation-associated complications (3). Barotrauma and volutrauma are key factors of ventilator-induced lung injury. The monitoring of tidal volume and inspiratory pressure appears therefore of paramount importance, even though evidence for clear targets for those variables is lacking in pediatric acute lung injury. The measurement of inspiratory pressure aims to reflect the pressure applied to the alveoli at the end of inspiration. During pressure-regulated ventilation, inspiratory pressure is relatively stable over inspiration, and peak pressure is usually considered to evaluate inspiratory pressure. In volume-controlled ventilator mode, the peak inspiratory pressure is strongly influenced by the resistance of the ETT and of the airways; in those cases, the plateau pressure better reflects the impact of ventilation on the poorly compliant lung. To measure the plateau pressure, a no-flow end-inspiratory pause (0.2–1 s) should be applied to allow pressure equilibration, in the absence of patient effort.

Of note, the transpulmonary pressure (difference between alveolar and pleural pressure) would be a more adequate reflection of lung strain and barotrauma (4). Although transpulmonary pressure is not routinely monitored, it is important to recognize conditions in which airway pressure poorly represents transpulmonary pressure. On the one hand, airway pressure tends to overestimate transpulmonary pressure when pleural pressure is particularly high (eg, obesity, hyperinflation, major fluid overload, and increased tone following acute brain injury). On the other hand, airway pressure underestimates transpulmonary pressure when pleural pressure is particularly low, ie, when the patient generates important spontaneous inspiratory efforts. In the latter condition, the resulting tidal volume should be closely monitored to detect risk of volutrauma.

Ventilators used in children with PARDS should display flow-time, pressure-time, and volume-time curves. The benefit of the analysis of these scalars has not been demonstrated in clinical practice, but it is relatively simple and provides some useful information. The expiratory phase examination permits detection of dynamic hyperinflation (inspiration occurring while expiration flow is not null) and expiratory flow limitation, a condition that may occur especially during ventilation with high respiratory rate for compensation of low tidal volumes, and relatively long inspiratory time. During volume-regulated ventilation, marked increase of peak pressure should alert for increased resistance, whereas increased plateau pressure suggests lowered compliance. During pressure-regulated ventilation, a loss of compliance will result in lower tidal volume. High expiratory flow during the early expiration is also a sign of poor compliance, with a fast time constant. Clear asymmetry between inspiratory and expiratory volume suggests significant air leak from the respiratory system. Noisy expiratory and inspiratory flows suggest the presence of tracheal secretions (5). Important asynchrony can also be diagnosed on these graphs, but this method is not sensitive (6). Flow-volume loops, which are available on certain ventilators, may also exhibit the characteristic pattern of expiratory flow limitation, but with limited reliability.

Quasi-static pressure-volume loop is the reference method to evaluate the compliance of the respiratory system, and the analysis of its hysteresis pattern has been considered as a potential tool to guide recruitment strategy and PEEP setting. In particular, the identification of a lower inflection point has been considered as an indication of alveoli recruitment during inflation (or derecruitment during deflation), leading to the theory to adapt PEEP above this point when it exists, whereas conditions without a lower inflection point were considered as not recruitable with PEEP. Several issues have, however, tempered this theoretical interest (7). First, technically, the acquisition of quasi-static pressure-volume loops is complex. To eliminate the resistive component in the pressure-volume relationship, a low flow (below 9 L/min) or sequential titration volumes (super syringe) should be used; specific high accuracy devices are necessary to conduct the maneuver and record the volume changes; the patient should be deeply sedated or paralyzed; and no leaks should be present around the tube. Second, interpretation of the loop can be difficult, especially for the identification of inflection points. Finally, the clinical benefits of using pressure-volume curves have not been confirmed in adults with acute respiratory distress syndrome, and no study has evaluated this issue in pediatric clinical practice.

During ventilation, most ventilators can display the dynamic pressure-volume curve without disconnection or setting changes. It is important to note that these loops are obtained with very high flow when compared with quasi-static loops, and the resistance component of the system has a major impact on the shape of the curve (7). Dynamic pressure-volume loops should, therefore, be looked at with caution. Intrabreath overdistension may be detected when the end inspiration part of the curve flattens, with a beaked shape. It has been shown in neonates and children that this flattening can be quantified to facilitate the diagnosis of overdistension, using the ratio of the compliance calculated during the final part (20%) of inspiration to the compliance of the entire tidal inspiration (C20/C) (8) or using the sign of the nonlinear *c* coefficient of a second-order polynomial equation fitted to the inspiratory pressure-volume curve (9). These calculation methods are, however, not available at the bedside, and the visual assessment of overdistension has not been validated. Another potential interest of pressure-volume loop relies on the observation of intrabreath recruitment (lower inflection point pattern), and in the follow-up of the shape of the loop, which may indicate compliance changes. The validity of these observations has not been evaluated in children with PARDS. The lower inflection point in this condition can be influenced by the resistance of the ETT (10, 11). Furthermore,

the frequent use of nonconstant inspiratory flow makes those findings even more complex to interpret.

Altered compliance is the predominant alteration in PARDS (12). Compliance measurement has many theoretical interests, including the assessment of severity (12), the follow-up of disease status, and the management of the ventilator settings and, in particular, PEEP adjustment (13). The quasi-static pressure-volume curve is the reference method to evaluate compliance of the respiratory system, but its use in clinical practice is complex as discussed above. A simpler approach is to evaluate the dynamic compliance using the ratio of exhaled tidal volume divided by the driving pressure, providing several precautions are undertaken. An end-inspiratory occlusion should precede this measurement when in volume control mode, to take into account the plateau pressure rather than the peak pressure in the driving pressure calculation; the patient should not be actively breathing; the exhaled tidal volume should be precisely measured (see below); the leak around the ETT should be minimal. It should be noted that PARDS is a heterogeneous disease, and the expiration pattern does not follow a single compartment model pattern. A nonlinear analysis or a multiple linear regression analysis should, therefore, be used to best evaluate the respiratory mechanics (14, 15). These recordings are not available at the bedside in clinical practice.

During ventilation with constant inspiratory flow, ie, volume control mode, the shape of the airway pressure-time curve during inspiration has been used to assess lung recruitability or distension, using the so-called stress index (16). Briefly, a downward concavity of the airway pressure (resulting in a stress index < 1) suggests that compliance increases through the inspiration, which may indicate that intrabreath recruitment occurs and that a higher PEEP may be necessary. On the other hand, a stress index higher than 1 reflects an upward concavity, suggesting a decrease in compliance during inspiration that could indicate overdistension. Specific equipment and a constant flow ventilation mode are necessary to use this approach. The stress index concept has not been evaluated in pediatric patients.

Intrinsic PEEP (PEEPi) can occur when the expiratory flow is limited, which may occur because of increased airways resistance or because the expiration is terminated early by the next inhalation. PEEPi generates hyperinflation, which may exacerbate the compliance loss, and increases the work of breathing because of difficulty in initiating the breath (17). Of note, infants younger than 1 year dynamically elevate their end-expiratory lung volume during normal breathing, using early termination of expiration, and expiratory flow braking by a laryngeal contraction and persistence of diaphragm activity during expiration (18). Abnormal PEEPi can be suspected with examination of the flow-time curve and can be quantified using an end-expiratory occlusion. This measure can help for PEEP adjustment, but it necessitates the absence of patient respiratory effort and the possibility to apply an end-expiratory pause. No pediatric study has evaluated the clinical benefit to measure PEEPi.

The location of measurement of flow and tidal volume is important. Although most modern ventilators have built in software to adjust for mechanical ventilator tubing compliance, tidal volumes measured at the proximal airway with a pneumotachograph can still be remarkably different than those measured at the mechanical ventilator (19). This problem is magnified with infants and smaller children, even when allowing for tubing compliance compensation (20, 21), with tidal volumes measured at the ventilator often being considerably different than those at the ETT. In addition, the shape of the expiratory portion of the tidal flow-volume curve is often distorted to an obstructed flow pattern when acquired in the ventilator rather than at the ETT, which may lead to incorrect ventilator management choices. Future mechanical ventilation protocols must consider the location of the tidal volume measuring device. Furthermore, given the common use of uncuffed tubes in children, tidal volume (and also resistance and compliance) measurements will not be accurate if there is a leak more than 18% around the ETT (22).

Respiratory System Variables Derived From Additional Monitoring. Esophageal manometry, in the acute phase of disease, permits calculation of the pressures that distend the alveoli. Esophageal pressure estimates the pleural pressure, and subsequently the calculation of the transpulmonary pressure differences at inspiratory pressure (peak or plateau, where appropriate) and at end-expiration (PEEP). In clinical practice, this monitoring may help to adjust the PEEP level and the inspiratory support, particularly in patients with suspected abnormal pleural pressure (eg, obesity, obstructed airways disease, major fluid overload, and intra-abdominal processes). One randomized trial evaluated this approach in adult patients with ARDS (23), reporting improved oxygenation and respiratory compliance over the first 72 hours compared with the ARDSnet PEEP/FIO_2 protocol.

Esophageal manometry, in the ventilator weaning phase of PARDS, permits us to calculate the work of breathing from PEEPi or any cause of decreased respiratory system compliance by using the Campbell diagram, or the pressure.rate product (PRP; esophageal pressure times respiratory rate) or pressure-time product, which are surrogates. A few small, controlled studies have suggested that it has a value (17, 24, 25). However, at this stage, the assessment of the work of breathing from pleural pressure monitoring is essentially reserved for research purposes although several modern ventilators allow its continuous monitoring.

The group who devised the Berlin Definition for adult ARDS felt that the measurement of deadspace was challenging. Instead, the panel chose minute ventilation standardized at a $PaCO_2$ of 40 mm Hg as a surrogate [$V'E_{CORR}$ = minute ventilation $\times$ $PaCO_2/40$]. A high $V'E_{CORR}$ (> 10 L/min) was evaluated further but ultimately not included. The equivalent pediatric value, standardized further to body weight, is approximately 150 mL/kg/min. This is largely a research tool in pediatric ARDS where only one group has prospectively documented an elevated value (mean approximately 250 mL/kg/min by interpolation) (26).

FRC is the only lung capacity that can be accurately, repeatedly, and reliably measured in patients unable to cooperate, such as ventilated patients of all ages. In ventilated patients,

FRC is affected by the mode of ventilation and the ventilator settings, such as PEEP, respiratory rate, and the ratio of the times of inspiration to exhalation (I:E ratio). Hence, its accurate measurement should increase our understanding of the respiratory pathophysiology and improve the management of ventilated children with physiologically appropriate strategies. FRC can be measured in the PICU by body plethysmography (27), gas dilution (usually helium), gas washout (usually nitrogen) (12, 28), and by a molar mass change technique (using sulfur hexafluoride or helium) (29, 30). A few pediatric studies in ARDS have confirmed a low FRC (28, 31) and one has documented a reduced total lung capacity (32) using a nitrogen washout technique. However, despite its potential to improve lung protective ventilation, the shortage of simple and automated bedside techniques has limited the acceptance of measuring FRC in the intensive care patient. Furthermore, the respective contribution of distension versus recruitment in FRC changes is not simple to distinguish. Only one modern ventilator offers a turnkey solution for FRC measurement, but it is unsuitable for pediatrics. Hence, the measurement of FRC remains largely a research application.

Continuous monitoring of Co_2 is recommended to assess the accuracy of ventilatory support, using end-tidal Co_2/time curves, volumetric capnographic/time curves, or transcutaneous Co_2 measurements, the latter being useful when end-tidal sampling is unavailable, eg, high-frequency ventilation (33). Capnography is simple to do in conventional ventilation (34), allowing calculation of clinically useful and predictive information such as the ratio of deadspace to tidal volume, end-tidal alveolar deadspace fraction (AVDSF), and Ventilation Index (35–37). Classically, the volumetric capnography output is displayed as a single curve repeated each breath while time-based end-tidal capnography is displayed as a continuous trace. The latter might give additional information if plotted in the same way as the volumetric trace, allowing for the "freezing" of plots intermittently whereby trends might be more easily identified. The ratio of deadspace to tidal volume can be measured using volumetric capnography and arterial or capillary Co_2, providing information on lung injury severity (26). The proportion of delivered tidal volume not participating in gas exchange constitutes V_D/V_T (comprised both alveolar and airway deadspace) and is calculated using the Enghoff modification of the Bohr equation. Similar information can be obtained using the end-tidal AVDSF where end-tidal Co_2 is substituted for the mixed expired Co_2 (36, 38) although there may be situations when AVDSF may not be a good surrogate for V_D/V_T, such as lower airway obstruction. There are stand-alone, bedside systems to undertake deadspace measurements, and the capability is built into some modern ventilators

There is increasing evidence that respiratory muscle dysfunction rapidly develops in mechanically ventilated critically ill adult patients, and that this dysfunction may prolong weaning. To decrease this complication, it has been advocated to maintain patient breathing efforts and to monitor the respiratory muscle function (39). Diaphragm dysfunction has been less studied in pediatric patients, and the benefit of such monitoring has not been demonstrated. Respiratory drive measurement is also used to evaluate extubation readiness.

The respiratory drive can be assessed quantifying the pressure developed against an occlusion during the first 100 ms of inspiration ($P_{0.1}$). This delay prevents any reaction from the patient in response to occlusion. $P_{0.1}$ has been used with success in critically ill children and correlates with other markers of ventilatory drive (40, 41). The value of $P_{0.1}$ in the evaluation of extubation readiness has been reported with conflicting results (40, 42–44).

Respiratory muscle function has also been studied in infants and children using esophageal balloon catheters for a variety of measurements including Tension-Time Index (42) and PRP (24, 25) as a surrogate for the work of breathing, with encouraging results. Both of these measures can be done on intubated and nonintubated patients, but clinically, the PRP is the easier measurement to obtain requiring simpler calculations.

TAA has also been used as a measure of effort of breathing, particularly in upper airway obstruction (45, 46) but also for extubation readiness (24). Unfortunately, at this time, it has not been shown that TAA monitoring can reliably predict respiratory fatigue in infants, children, and adults with severe respiratory diseases.

The EAdi can be quantified in clinical practice using a validated technology developed for the neurally adjusted ventilator assist mode of ventilation. EAdi also reflects the respiratory drive and is correlated with $P_{0.1}$ (40). The monitoring of EAdi could facilitate the detection of conditions of overassistance with absent ventilator effort, conditions of excessive efforts, and patient-ventilator asynchrony (47). Increased EAdi during expiration period may suggest increased efforts of the patient to elevate his/her end-expiratory lung volume (18). Conflicting results have been reported in the evaluation of extubation readiness (40, 48).

The use of ultrasonography to quantify diaphragm function is increasingly reported in mechanically ventilated adults. This bedside tool allows quantification of diaphragmatic movement, force, and changes in diaphragmatic thickness during inspiration, which may facilitate the diagnosis and follow-up of diaphragm weakness (49). The use and performance of this tool in children with acute respiratory failure remain to be evaluated.

OXYGENATION PARAMETERS, SEVERITY SCORING, AND Co_2 MONITORING

Recommendations

6.3.1 Monitoring of Fio_2, Spo_2, and/or Pao_2, mean airway pressure, and PEEP is recommended to detect PARDS, to assess PARDS severity, and to guide the management of oxygenation failure. *Strong agreement*

6.3.2 We recommend that blood pH and $Paco_2$ measurement frequency should be adjusted according to PARDS severity, noninvasive monitoring data, and stage of the disease. *Strong agreement*

6.3.3 Peripheral venous blood gas sampling is not recommended. *Weak agreement (83% agreement)*

6.3.4 Continuous monitoring of Co_2 is recommended in children with invasive mechanical ventilation, using end-tidal Co_2/time curves, volumetric capnography, and/or transcutaneous Co_2 measurements. *Strong agreement*

Rationale

Regular analysis of arterial or capillary blood gas is important to assess PARDS severity and to adjust ventilator support. Blood gas frequency should be adjusted according to PARDS severity and stage of the disease. At present, even with the availability of continuous oxygen saturation and end-tidal carbon dioxide values, four hourly blood gas sampling seems the norm (50). Peripheral venous blood gas does not accurately predict arterial gas. Although transcutaneous oxygen monitoring has little application in pediatric practice, similar Co_2 monitoring has a role (51, 52) (*vide supra*), particularly during high-frequency modes of ventilation where end-tidal Co_2 values are not available (33, 53). End-tidal Co_2 monitoring is simple to do (34) and allows calculation of clinically useful and predictive information (35, 36). The gap between end-tidal and arterial Co_2 is more important in sicker patients with larger deadspace volume and may change over time. Therefore, for patients with larger deadspace as expected in the acute phase of PARDS, end-tidal Co_2 cannot be used as a reliable surrogate for arterial or capillary Co_2 until a correction method is validated (54).

At a minimum, monitoring of Fio_2, Spo_2, peak inspiratory pressure, mean airway pressure, and PEEP is recommended to detect PARDS, to assess PARDS severity, and to guide the management of oxygenation failure using lung protective ventilation strategies. Various scores permit the assessment of the severity of PARDS and prediction of mortality (36, 55–57). Provided Spo_2 is less than 98%, the Spo_2/Fio_2 ratio, Oxygen Saturation Index (55), and noninvasive pediatric lung injury score (58, 59) are validated noninvasive scores. Pao_2/Fio_2 ratio, Oxygenation Index (55), alveolar-arterial oxygen gradient, arterial-alveolar oxygen ratio, pediatric lung injury score (55) necessitate an arterial Pao_2. Ventilation Index (37), end-tidal AVDSF (36), and deadspace-tidal volume ratio (38) require either an arterial or a capillary Pco_2.

Arterial blood gases (pH, Pao_2, and $Paco_2$) can be continuously monitored using special arterial catheters, mostly in a research context, but also during extracorporeal membrane oxygenation. Although several prospective studies in neonates (60), older infants, and children (61, 62) attest to the accuracy and reproducibility of the one intra-arterial device (Paratrend 7; Diametrics Medical, High Wycombe, United Kingdom), which was clinically available, it has subsequently been withdrawn and no comparable devices exist today for continuous radial or femoral intra-arterial sampling.

SPECIFIC WEANING CONSIDERATIONS

Recommendations

6.4.1 We recommend at least daily assessment of predefined clinical and physiological criteria of extubation readiness to avoid unnecessary prolonged ventilation. *Strong agreement*

6.4.2 We recommend that spontaneous breathing trials and/or extubation readiness tests (ERTs) should be performed. *Strong agreement*

6.4.3 We recommend that, for research studies, Spontaneous Breathing Trials and ERTs should be standardized. *Strong agreement*

Rationale

Concerning ERT, no criteria have been validated to discriminate extubation success and failure. In addition to clinical signs of respiratory tolerance, several measurements may be useful in clinical practice, including rapid shallow breathing index (63, 64), compliance resistance oxygenation pressure index (64), work of breathing measures (such as PRP [24] and tension-time index [42]), and volumetric capnography (35).

This subject has been recently reviewed in depth (65). The successful achievement of the ERT should be the endpoint of mechanical ventilation for the purpose of pediatric trials. This is likely a better endpoint of assisted ventilation than actual extubation given the relatively high incidence of postextubation upper airway obstruction (66), requiring further ventilator assistance either noninvasively or via ETT, which spuriously prolongs the length of ventilator assistance for PARDS.

An ERT should include an assessment of clinical factors and physiological ones and allow for a testing of both respiratory muscle strength and endurance. Few ERT trials with adequate numbers of patients have been undertaken and have resulted in higher failed extubation rates (approximately 14%) (67, 68) as opposed to clinical judgment alone (4–6%) (65). This should be an important area of research.

Spontaneous breathing trials and extubation readiness tests should be systematically performed as soon as predefined clinical and physiological criteria are achieved, using either continuous positive airway pressure, a low level of pressure-support ventilation (maximum of 5/5 cm H_2O) or T-piece ventilation, to avoid unnecessary prolonged length of ventilation (65). However, the only study to date, which has evaluated this approach (in two centers), demonstrated a 20% recourse to noninvasive ventilation and a 14% reintubation rate within 48 hours, in both study and control arms (69).

IMAGING

Recommendations

6.5.1 We recommend that chest imaging is necessary for the diagnosis of PARDS, and to detect complications such as air leak or equipment displacement. Frequency of chest imaging should be predicated on patient clinical condition. *Strong agreement*

6.5.2 There is insufficient evidence to recommend the systematic use of chest CT scan, lung ultrasonography, and electrical impedance tomography (EIT). *Strong agreement*

Rationale

A chest radiograph is initially important to establish the diagnosis of PARDS, even if its interpretation is difficult with large interobserver variability (70). It is generally repeated regularly

to monitor the progression of the disease, detect complications, and check the correct position of tubes and catheters. The optimal frequency of obtaining chest radiographs in children with PARDS is not established. Some studies conducted in adult ICUs suggest that an on-demand strategy could safely replace the routine daily radiograph strategy (71, 72). However, this approach may not be transposable to children with acute respiratory failure, in whom half of routine chest x-rays are followed by an intervention (73). Interventions are less frequent when the number of devices is lower and in children less than 40 kg (73).

Chest CT scan may be necessary in PARDS to help with the etiological diagnosis or to diagnose certain complications. Its role as a monitoring tool to guide the recruitment management has been suggested in studies in adult populations (74). In PARDS, a single study including six patients reported the feasibility of evaluation of lung aeration by CT scan following a recruitment maneuver (75). The clinical impact of assessment of lung aeration remains to be studied, whereas the risks related to patient transport and irradiation are not negligible. CT scan in PARDS should, therefore, be restricted to specific clinical indications, or to clinical research.

Lung ultrasonography is a simple and validated method to evaluate pleural effusion in adults and children (76). It is also increasingly used in adults with ARDS to detect lung complications and to evaluate lung recruitment (76), with the advantages of lower radiation exposure, increased repeatability, and at least as good performance when compared with radiography (77). Data in children with PARDS are limited to a retrospective study of nine patients, in whom lung recruitment observed by ultrasonography seemed correlated with oxygenation improvement (78). Additional studies are warranted to confirm the validity and use of this technique in this indication.

EIT is a recent noninvasive imaging tool, which permits bedside dynamic visualization of volume changes in the different lung regions. Most pediatric data in PARDS have been reported by a single team in six and 10 patients (79, 80). EIT was feasible and demonstrated striking heterogeneity in regional ventilation during assisted ventilation and during recruitment or derecruitment maneuvers. Differential EIT patterns were evidenced between recruitment responders and nonresponders, and important overdistension of non-dependent regions was frequently observed (79). This technology appears, therefore, promising to guide the management of mechanical ventilation and the recruitment strategy, but further validation studies are clearly needed to delineate its clinical interest and optimal indications.

HEMODYNAMIC MONITORING

Recommendations

6.6.1 Hemodynamic monitoring is recommended during PARDS, in particular, to guide volume expansion in the context of fluid restrictive strategy, to evaluate the impact of ventilation and disease on right and left cardiac function, and to assess oxygen delivery. *Strong agreement*

6.6.2 In patients with suspected cardiac dysfunction, echocardiography is recommended for noninvasive evaluation of both left and right ventricular function, the preload status, and pulmonary arterial pressures. *Strong agreement*

6.6.3 We recommend that a peripheral arterial catheter should be considered in patients with severe PARDS for continuous monitoring of arterial blood pressure and arterial blood gas analysis. *Strong agreement*

6.6.4 There is insufficient evidence to recommend the systematic use of the following hemodynamic monitoring devices: pulse contour with transpulmonary dilution technology, pulmonary artery catheters (PACs), alternative devices to monitor cardiac output (CO) (ultrasonic CO monitoring, transesophageal aortic Doppler, noninvasive monitoring of CO based on changes in respiratory Co_2 concentration caused by a brief period of rebreathing), central venous oxygenation monitoring, and B-type natriuretic peptide (BNP) measurements. *Strong agreement*

Rationale

During severe PARDS, interactions between lung and cardiac function are of paramount importance. Briefly, the right ventricular function may be directly impaired by the presence of pulmonary hypertension related to the lung disease and/or the impact of elevated airway pressures (in particular, PEEP); left heart function may also be influenced by interventricular dependence, by a direct effect of the disease, or in the setting of multiple organ dysfunctions. During PARDS, many actions are frequently taken to improve arterial oxygenation, but the importance of CO as a major determinant of oxygen transport must absolutely be taken into account in those decisions. Finally, the volume status of these patients is also a major issue. Although volume expansion may be necessary, especially in the context of elevated intrathoracic pressure and capillary leak syndrome, fluid overload is very frequent, severe, and clearly associated with a worse outcome (81–83). Consequently, the evaluation of hemodynamic status is a key component in the management of children with PARDS.

Indwelling arterial catheters are usually installed to monitor continuously the blood pressure and to facilitate arterial blood gas draws. The rate of complications associated with arterial catheters must be taken into account (3–10%) (84–86) but seems outweighed by the benefits especially in the acute phase in these particularly unstable patients. In an observational study including more than 12,000 children with mechanical ventilation, it appears that less than 85% of the patients were equipped with such monitoring, but presumably the ones with arterial catheters were the more severely ill (87). An arterial catheter should be removed as soon as its necessity is not clear. Of note, many data from adult literature suggest that the use of pulse pressure variation to predict fluid responsiveness is poorly reliable during severe ARDS (88). This has not been studied in children, but a cautious approach appears warranted.

Echocardiography permits evaluation of the left and right ventricular function, to estimate the pulmonary pressures and to assess the volume status. It is a discontinuous, but noninvasive, technology. A study reporting 103 examinations conducted in children with PARDS confirmed its feasibility (89). The clinical impact of using echocardiography during management of children with PARDS has not been reported.

TABLE 2. Other Parameters That May be Monitored in the Management of a Children With Acute Respiratory Distress Syndrome

Parameter	Clinical Information	Phase of the Disease	Continuous or Intermittent Monitoring	Required Monitor and Equipment	Risk	Recommendation for Monitoring Use
Respiratory system variables derived from measurement in airway circuit						
Flow-volume loop	Expiratory resistance, flow limitation	Acute	Intermittent	Ventilator	None	May help in clinical practice
Pressure-volume curve: static	Estimation of static compliance Severity evolution Overdistension detection PEEP adjustment	Acute	Intermittent	Ventilator with special function. Paralysis or deep sedation	Minimal	Research
Pressure-volume curve: Dynamic	Estimation of dynamic compliance and resistance Severity evolution Overdistension detection PEEP adjustment	Acute	Intermittent	Ventilator	None	May help in clinical practice
Compliance and resistance: dynamic	Severity evolution (part of the lung injury score) PEEP and timing adjustment	Acute	Intermittent	Ventilator Leak around endotracheal tube $< 18\%$	None	Mostly research
Stress index	Assessment of distension PEEP adjustment	Acute	Intermittent	Ventilator constant flow volume-controlled mode	None	Research
Intrinsic PEEP	PEEP and ventilator timing adjustment	Acute	Intermittent	Ventilator Expiratory occlusion Paralysis or deep sedation	Minimal	May help in clinical practice
Respiratory system variables derived from additional monitoring						
Esophageal manometry	Calculation of transpulmonary pressure during inspiration and at end expiration PEEP adjustment Prevention of ventilator-induced lung injury	Acute	Continuous	Esophageal balloon Pressure monitor or ventilator	Minimal	May help in clinical practice
Work of breathing Pressure-rate product	Adequacy of support	Acute	Intermittent	Esophageal balloon Pressure monitor or ventilator	Minimal	Research
Corrected minute ventilation	Severity assessment	Acute	Intermittent	Ventilator ABG or CBG	None	Research
Functional residual capacity	Severity assessment PEEP adjustment	Acute	Intermittent	Ventilator with special function or dedicated device	Minimal	Research
Ratio deadspace/tidal volumes (V_D/V_t)	Severity assessment and evolution Weaning success indicator	All	Intermittent	Volumetric capnography ABG or CBG	Minimal	May help in clinical practice
Alveolar deadspace fraction	Severity assessment and evolution	All	Intermittent	Volumetric or time-based capnography ABG or CBG	Minimal	May help in clinical practice

(*Continued*)

TABLE 2. (*Continued*). Other Parameters That May be Monitored in the Management of a Children With Acute Respiratory Distress Syndrome

Parameter	Clinical Information	Phase of the Disease	Continuous or Intermittent Monitoring	Monitor and Equipment	Risk	Recommendation for Monitoring Use
Oxygenation parameters and severity score						
Pao_2/Fio_2 Spo_2/Fio_2	Severity assessment Diagnosis	All	Intermittent	ABG	Minimal	May help in clinical practice
Oxygenation index, oxygen saturation index	Severity assessment	Acute	Intermittent	ABG, ventilator	Minimal	May help in clinical practice
Continuous arterial gas monitoring	Ventilator settings adjustment	All	Continuous	Specific arterial catheter	Minimal	Research
Lung injury score Noninvasive lung injury score	Severity assessment	Acute	Intermittent	Chest x-ray ABG Compliance	Minimal	Mostly research
Ventilation index	Severity assessment	Acute	Intermittent	ABG, or CBG	Minimal	Research
Respiratory muscle activity						
$P_{0.1}$	Respiratory drive	Acute	Intermittent	Ventilator with specific function	None	Research
Esophageal pressure.rate product	Respiratory drive	Acute	Continuous	Esophageal balloon Pressure monitor or ventilator	Minimal	May help in clinical practice
Electrical activity of diaphragm	Respiratory drive (phasic activity) PEEP adjustment (tonic activity)	All	Continuous	Ventilator with specific function Special nasogastric tube	Minimal	Research
Respiratory inductance plethysmography	Thoracoabdominal synchrony Volume variations	Acute	Continuous	Plethysmograph Thoracic and abdominal circumferential bands	Minimal	Research
Ultrasonography of diaphragm	Detection of diaphragm weakness	All	Intermittent	Ultrasound	None	Research
Specific weaning considerations						
Rapid shallow breathing index	Weaning tolerance	Weaning	Intermittent	Clinical signs Ventilator	None	May help in clinical practice
Compliance resistance oxygenation pressure index	Weaning tolerance	Weaning	Intermittent	ABG, Dynamic compliance Negative inspiratory pressure	Minimal	May help in clinical practice
Pressure.rate product	Weaning tolerance Work of breathing	Weaning	Continuous	Esophageal pressure	Minimal	Research

(*Continued*)

TABLE 2. (*Continued*). Other Parameters That May be Monitored in the Management of a Children With Acute Respiratory Distress Syndrome

Parameter	Clinical Information	Phase of the Disease	Continuous or Intermittent Monitoring	Monitor and Equipment	Risk	Recommendation for Monitoring Use
Imaging						
Chest CT scan	Etiological diagnosis PEEP adjustment (homogeneity, recruitability)	Acute	Intermittent	CT scan Transport	Moderate	Mostly research
Lung ultrasonography	Etiological diagnosis PEEP adjustment (recruitment) Weaning	All	Intermittent	Ultrasound	None	Mostly research
Electrical impedance tomography	PEEP adjustment (homogeneity, recruitability)	Acute	Intermittent	Electrical impedance tomography stand-alone device or ventilator with specific function	Minimal	Mostly research
Hemodynamic monitoring						
Continuous monitoring of arterial pressure	Hemodynamic status Blood gas	All	Continuous	Arterial catheter	Minimal	Likely helps in clinical practice
Pulse index continuous cardiac output	Cardiac output Volume responsiveness Extravascular lung water	Acute	Continuous	Specific arterial catheter Specific monitor Central venous access	Minimal	May help in clinical practice Research
Echocardiography	Cardiac output Pulmonary pressure Volume responsiveness	Acute	Intermittent	Ultrasound	None	Likely helps in clinical practice
Ultrasonic cardiac output monitor	Cardiac output, systemic vascular resistance index, Inotropy Index	Acute	Intermittent	Ultrasound	None	Mostly research
Pulmonary artery catheter	Cardiac output Pulmonary pressure Adequate oxygen transport/consumption	Acute	Continuous	Pulmonary artery catheter	Moderate	May help in specific cases
$Scvo_2$	Balance oxygen transport/ consumption	All	Continuous or intermittent	Conventional or specific central venous access	Minimal	May help in clinical practice
Tissue o_2/ near-infrared spectroscopy	Adequate oxygen transport/consumption	All	Continuous	Specific monitor	None	Research
Brain natriuretic peptide	Fluid balance Cardiac dysfunction participation in the lung injury	All	Intermittent	Laboratory	None	May help in clinical practice

PEEP = positive end-expiratory pressure, ABG = arterial blood gas, CBG = capillary blood gas, SpO_2 = pulse oxygen saturation, $ScvO_2$ = central venous oxygen saturation.

The pulse index continuous CO (PiCCO) device, which combines a transpulmonary thermodilution technology with arterial pulse contour analysis, has been shown accurate to evaluate cardiac index and cardiac preload in children, assuming regular recalibration of pulse contour analysis (90). However, no validation studies have been conducted specifically in PARDS. Theoretically, one can expect that measurements of cardiac index and static indices of preload status should remain reliable in PARDS, but it is highly possible that pulse contour-derived variables may not be accurate due to the respiratory system condition and low tidal volume. This technology is referred to as minimally invasive because it necessitates a specific femoral arterial catheter, and a central venous catheter ideally in supradiaphragmatic position. The benefit/risk ratio of PiCCO monitoring remains to be studied.

PiCCO also provides an intermittent estimation of extravascular lung water through transpulmonary thermodilution measures, and an index of pulmonary vascular permeability can be calculated. Validation studies of extravascular lung water accuracy in pediatric animal models of PARDS are still pending. A prospective multicenter study in 266 adults with ARDS showed that these indices correlates with oxygenation parameters and with outcome (91). In children, one study conducted in 24 mechanically ventilated children with various diseases found no association between extravascular lung water and oxygenation parameters or x-ray findings (92). On the other hand, a study conducted in 27 children with PARDS reported significantly lower extravascular lung water at baseline in survivors when compared with nonsurvivors (93). Extravascular lung water significantly decreased over the first day in survivors only. Furthermore, extravascular lung water was correlated with fluid overload (93). An important issue with extravascular lung water estimation is that its normal value is not known and seems dependent on age because the relationship between cardiac preload and intrathoracic blood volume significantly changes, particularly before 2 years of age (94). Additional validation studies are therefore warranted before PiCCO monitoring could be recommended with specific therapeutic aims in children with PARDS.

For the management of patients with severe respiratory failure, physicians titrate medical therapies and mechanical ventilation with the goal of optimizing oxygen delivery through normalization of CO and systemic vascular resistance. Thermodilution using a thermistor-tipped pulmonary artery flotation catheter is an accepted standard for cardiac index measurement and has been used for many years in children (95). Small versions of the pulmonary artery flotation catheter are suitable for transvenous placement in smaller children. There are risks involved in that invasive procedure, not only in the placement in children (96) but also in the reliable interpretation of the results. Recently, the use of PAC in children has been extensively reviewed (97), with the conclusion that a high level of evidence supports the use of PAC in selected pediatric patients, especially those with pulmonary arterial hypertension and shock refractory to standard fluid resuscitation and vasoactive agents. There are no data to suggest that the use of a PAC increases mortality in children. Studies concerning the use of a PAC, specifically in PARDS, are few (98, 99) but no complications were reported.

Ultrasonic CO monitor is a new and widely available technology using continuous wave Doppler echocardiography. It provides a noninvasive, easy to use, objective, bedside alternative to thermodilution techniques (100). In numerous newborn infants (101, 102), and in mechanically ventilated adults (103) and children (104), it was found to be a simple and reliable technique to follow changes in CO, when the operator is appropriately trained. Further evaluation of its role in PARDS is needed .

Mixed central venous oxygen saturation ($Scvo_2$) measurement from a central venous catheter placed close to, or within, the right atrium, as a surrogate for mixed venous oxygen saturation is simple and clinically accessible. Compared with CO measurement, $Scvo_2$ is more directly related to tissue oxygenation. Furthermore, when tissue oxygenation is a clinical concern, $Scvo_2$ is less prone to error when compared with CO, where small measurement errors may lead to larger errors in interpreting adequacy of oxygen delivery. An $Scvo_2$ goal value greater than 70% is recommended for hemodynamic support of pediatric and neonatal septic shock patients (105). There are a few supportive studies in pediatric sepsis for this continuous monitoring modality (106, 107), but none specifically in PARDS. A large study in adults with ARDS comparing PAC with $Scvo_2$ catheter measurements for fluid management found no advantage of the PAC (108).

Near-infrared spectroscopy (NIRS) is a noninvasive means of assessing tissue oxygenation through optical quantification of local deoxygenated and oxygenated hemoglobin. NIRS is increasingly used as a hemodynamic monitor in critically ill patients (109, 110). Evaluation of tissue oxygenation with NIRS can be misleading in the presence of microcirculatory abnormalities, which can occur during severe respiratory disease (111), necessitating dynamic testing (vascular occlusion) rather than absolute value readings. The latter approach is more complex and rarely reported in children. The additive value of NIRS monitoring during PARDS management has not been reported and remains questionable.

BNP is a biomarker produced by the cardiac ventricles in response to myocyte stretch. It has been proven useful in distinguishing cardiac and pulmonary causes of acute respiratory failure in adult and pediatric patients (112). As a biomarker of cardiac overload, BNP monitoring may be of theoretical interest in the management of PARDS, in particular, to guide volume expansion, to detect associated heart failure, and to evaluate the tolerance of ventilation weaning. This hypothesis is supported by a multicenter randomized controlled trial conducted in adults during the weaning phase, which showed that a BNP-guided management permitted decreasing the fluid overload and reducing the duration of mechanical ventilation. In PARDS, a prospective observational study including 48 children has evaluated the importance of BNP measurement at day 1 (113). Mean (±SD) BNP was 109 pcg/mL (± 311 pcg/mL), and higher BNP was associated with increased severity of illness, longer mechanical ventilation duration, and need for inotropic support. These data support the significance of elevated BNP, but further research is needed to assess the clinical benefit of BNP monitoring in children with PARDS.

RESEARCH PRIORITIES

During the last Pediatric Acute Lung Injury Consensus Conference meeting in Paris, several priorities for future research were identified. Generally speaking, there was interest regarding monitoring strategies, which would allow for better adapting ventilation to patient characteristics.

Choice of the body weight calculation for ventilator settings. Body weight is used in pediatric practice to standardize a number of measurements related to mechanical ventilation (tidal volume, compliance, rapid shallow breathing index, FRC, etc). Although pediatric practice is not entirely clear, it appears that actual body weight is most commonly used to calculate exhaled tidal volume. However, obesity is a problem in pediatric practice, as is failure to thrive with low weight for age and height. In addition, contractures and spinal deformities make direct measurement of length irrelevant. Formulae are now available to use ulna length as a determinant of height from birth to 19½ years (1, 2) and from Centers for Disease Control and Prevention & World Health Organization growth grids; this height can be used to find the IBW to which tidal volume can be targeted. Nonetheless, it is not known whether the lungs fail to grow appropriately when a child fails to thrive or whether the lungs are large if the child is obese. Prospective investigation of measured lung volume compared with that predicted from actual versus IBW in children, and whether the use of IBW has an effect on outcome in PARDS, is a priority. A recent meta-analysis of observational studies (114) suggests that unlike the ARDSNet trial in adults (115), tidal volume is not associated with mortality in pediatrics, and prospective interventional trials are crucially needed in this area.

Lung compliance monitoring: although there is insufficient evidence to recommend the systematic monitoring of many of the parameters of respiratory system mechanics, some are worthy of consideration for further research. Altered compliance is the predominant abnormality in PARDS (12). Compliance measurement has practical applications including the assessment of severity as shown in lung injury scores (12, 116), follow-up of the disease status, and the management of the ventilator settings and, in particular, PEEP adjustment (13). The evaluation of compliance (and particularly during over- and underinflation) is implicit in the measurement of the pressure-volume loops and PEEP defines, in part, the end-expiratory lung volume. Turnkey techniques for the measurement of dynamic compliance and lung volume (both FRC and TLC) under differing modes of ventilation (15, 28) would allow for their more complete investigation of roles and value in protective ventilation strategies.

Esophageal pressure monitoring: the role of transpulmonary pressure measurements in dealing with situations where there is reduced chest wall compliance (an unknown incidence in pediatric practice) at PEEP and plateau pressure needs to be investigated in pediatric mechanical ventilation because of its potential to determine over- and underinflation. At the same time, the likely effect of increasing usual PEEP levels if transpulmonary pressures at PEEP are followed mandates that an investigation of effects on CO (preferably by noninvasive techniques) also be undertaken. Esophageal pressures (alone or, more likely, as a part of the pressure and respiratory rate product) may also have a role in studies by acting as a surrogate for determining the work or effort of breathing to define the end of the lung disease process and suitability for extubation, excluding the possibility of upper airway obstruction from subglottic edema.

Deadspace evaluation: the ratio of deadspace to tidal volume (V_D/V_T) reflects pulmonary perfusion and signifies the effects of PEEP on both opening of collapsed alveoli and overdistension of alveoli. If alveolar opening occurs with increasing PEEP, in theory shunt decreases, resulting in lower calculated V_D/V_T. With further increases in PEEP, alveolar and airway overdistension should occur and true V_D/V_T will increase. If an elevated PEEP level decreases CO, V_D/V_T also increases due to decreasing pulmonary perfusion (36). Thus, V_D/V_T may be uniquely suited to balance cardiac and respiratory support during PEEP titration and should be further investigated.

Noninvasive blood pH predictor: although pulse oximetry has become an important technology for the noninvasive evaluation of oxygenation and has been successfully used in lung injury scores (59) and decision support tools for mechanical ventilation (50), we have no noninvasive counterpart for the prediction of pH for similar application. Via its relationship to pH through the Henderson-Hasselbalch equation, PCO_2 is a candidate. However, as noted previously, because of the "shunt" effect of atelectatic alveoli, end-tidal Co_2 cannot be used as a reliable surrogate for arterial or capillary Co_2 in ARDS until a correction method is validated (117) The situation with transcutaneous Co_2 is similar although new technologies may make this measurement more reliable. The quest for a noninvasive predictor of pH in pediatrics is an attractive area of research.

Evaluation of the impact of ventilation on cardiac function: in PARDS, hemodynamic monitoring appears of paramount importance although it has been much less evaluated when compared with respiratory mechanics monitoring. The impact of ventilation on right and left ventricular function, on pulmonary hypertension, and on preload condition, should be important considerations when making a decision regarding ventilator adjustment. As described above, the use of several monitoring devices has been reported, including echocardiography, PiCCO, ultrasonic CO monitor, $ScvO_2$, and NIRS. However, the validity and the clinical impact of these technologies should clearly be further evaluated.

EIT allows a noninvasive visual assessment of regional ventilation and seems feasible in children (79, 80). EIT has, therefore, some theoretical interest for PEEP titration, guiding recruitment while detecting overdistension, assessing lung heterogeneity and its evolution after ventilator settings changes. Additional work is needed to confirm its feasibility and clinical impact.

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APPENDIX 1. Pediatric Acute Lung Injury Consensus Conference Group

Organizing Committee: Philippe Jouvet, University of Montreal, Canada; Neal J. Thomas, Pennsylvania State University; Douglas F. Willson, Medical College of Virginia.

Section 1, Definition, incidence, and epidemiology: Simon Erickson, Princess Margaret Hospital for Children, Australia; Robinder Khemani, University of Southern California; Lincoln Smith, University of Washington; Jerry Zimmerman, University of Washington.

Section 2, Pathophysiology, co-morbidities and severity: Mary Dahmer, University of Michigan; Heidi Flori, Children's Hospital & Research Center Oakland; Michael Quasney, University of Michigan; Anil Sapru, University of California San Francisco.

Section 3, Ventilatory support: Ira M. Cheifetz, Duke University; Peter C. Rimensberger, University Hospital of Geneva, Switzerland.

Section 4, Pulmonary specific ancillary treatment: Martin Kneyber, University Medical Center Groningen, Netherlands; Robert F. Tamburro, Pennsylvania State University.

Section 5, Non-pulmonary treatment: Martha A. Q. Curley, University of Pennsylvania; Vinay Nadkarni, University of Pennsylvania; Stacey Valentine, Harvard University.

Section 6, Monitoring: Guillaume Emeriaud, University of Montreal, Canada; Christopher Newth, University of Southern California.

Section 7, Noninvasive support and ventilation: Christopher L. Carroll, University of Connecticut; Sandrine Essouri, Université Pierre et Marie Curie, France.

Section 8, Extracorporeal support: Heidi Dalton, University of Arizona; Duncan Macrae, Royal Brompton Hospital, England.

Section 9, Morbidity and long-term outcomes: Yolanda Lopez, Cruces University Hospital, Spain; Michael Quasney, University of Michigan; Miriam Santschi, Université de Sherbrooke, Canada; R. Scott Watson, University of Pittsburgh.

Literature Search Methodology: Melania Bembea, Johns Hopkins University.