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IAP Updates & Guidelines

Pediatric Critical Care 2024

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SECTION 1

Respiratory System

Section Editor: **Farhan AR Shaikh**

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1 Defining Pediatric Acute Respiratory Distress Syndrome

Deepak R, Farhan AR Shaikh

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a clinical syndrome with no distinct histopathology which is consistent in all cases, and creating diagnostic criteria should be dependent upon the hallmark signs and symptoms of the disease such as hypoxemia and on the pathophysiology like the loss of respiratory system compliance and functional residual capacity which can be diffuse or heterogenous, endothelial dysfunction, and alveolar epithelial dysfunction manifesting as interstitial and alveolar edema that increases the alveolar dead space. Ashbaugh et al. were the first to identify this constellation of symptoms and coin the term adult respiratory distress syndrome in 1967.[1] There was no consensus on the diagnosis of this condition until John Murray in 1988 proposed the lung injury score (LIS) where evidence of consolidation on chest X-ray (CXR), the degree of hypoxemia based on PaO_2/FiO_2 (PF) ratio, the compliance of the lung, and the need of peak end expiratory pressure (PEEP) in those who were ventilated were used to arrive at the diagnosis of ARDS.[2] In 1994, the American European Consensus Conference (AECC) definition adopted a standardized approach to diagnosis of ARDS for both clinical and research purposes.[3] The AECC definition required the hypoxemia of acute onset without definition of a time frame, presence of bilateral infiltrates on a CXR, and an absence of left atrial hypertension usually needing a pulmonary artery capillar wedge pressure (PACWP) <18 mm Hg by using a PA catheter. It split the diagnosis based on PF ratio of <300 mm Hg irrespective of PEEP value into acute lung injury and those with PF <200 mm Hg into ARDS. Although this definition had limitations like incongruency in interpreting bilateral infiltrates on CXR, modification in PF ratio if PEEP was varied, and a need for a PA catheter insertion to measure the PACWP, this was still followed through the whole time frame of ARDSNet trials for 20 years till the introduction of the Berlin definition in 2013.

BERLIN DEFINITION

At the start of this past decade, the Berlin definition of ARDS in 2013 was formulated.[4,5] In their definition, they clarified the timing of the disease to acute meaning <7 days from known clinical insult. The PACWP criteria were done away with by defining that the origin of lung edema causing respiratory failure was not explained completely by cardiac failure or fluid overload but if there was a concern of a cardiac

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risk they would use an echocardiogram to ascertain cardiac dysfunction. The CXR criteria were kept, as were the PF ratio criteria but with a significant modification of application of at least 5 mm Hg of PEEP or continuous positive airway pressure (CPAP) when calculating the PF ratio. They also reclassified the severity of the disease into mild-, moderate- and severe-ARDS using PF ratios of <300, <200, and <100 mm Hg, respectively. This definition was validated in a population >18 years of age, and we use to extrapolate these criteria to apply for pediatric patients to diagnose ARDS.

PALICC

The Pediatric Acute Lung Injury Consensus Conference (PALICC) group first met in 2012 to propose a more pediatric-specific guideline for the diagnosis of pediatric acute respiratory distress syndrome (PARDS) and in 2015, it came up with diagnostic criteria that are more practical to be applied in pediatric populations.[6] The timing of onset within 7 days of an insult and the cause of respiratory failure not fully explained by cardiac failure or fluid overload criteria were kept identical to the Berlin definition. The first change was in the chest imaging criteria that got rid of the requirement for bilateral opacities and simply needed a new infiltrate or an infiltrate consistent with pulmonary parenchymal disease. The second major change was, in children on mechanical ventilation, proposing the use of oxygen index (OI) instead of PF ratio as a better marker of hypoxemia and inclusion of oxygen saturation index (OSI) using pulse oximetry in children without invasive arterial lines but on mechanical ventilation to diagnose PARDS. It also proposed the use of the SpO_2/FiO_2 (SF) ratio to classify the degree of hypoxemia in children who were on noninvasive ventilation (NIV) and gave them criteria based on SF ratios to define at risk of PARDS. The severity criteria were based on an internal data review from Los Angeles study where they found a spike in mortality between OIs of 4 and 8, a second higher spike between OIs of 8 and 16, and the third highest spike after OI >16. These breakpoints were used to classify the disease into mild (OI 4–8), moderate (OI 8–16) and severe (OI >16) PARDS. The last criterion was to exclude the neonatal age group with perinatal lung insult. The criteria provided for the possibility of PARDS in special populations like cyanotic heart disease (CHD), chronic lung disease (CLD), or left heart failure where they meet the criteria of PARDS and their underlying disease cannot completely explain the deterioration.

In the PARDIE study published in 2018, PALICC definition was compared with Berlin definition in the same population across many centers all over the world.[7] In their study, of the 708 patients who met PALICC PARDS criteria (17.1% mortality), 230 (32.5%) concurrently met all Berlin criteria for ARDS (bilateral infiltrates on chest imaging and arterial PF ratio ≤300) at the time of PALICC PARDS diagnosis [26.5% (61/230) mortality]. An additional 183 (25.9%) met Berlin criteria in the subsequent 3 days after the initial PARDS diagnosis [20.8% (38/183) mortality] and 295 (41.7%) did not meet Berlin criteria within 3 days of PARDS diagnosis [7.5% (22/295) mortality]. They also found that, based on hypoxemia severity at PARDS onset, mortality was similar among NIV, mild, or moderate PARDS (10–15%) but higher for severe PARDS (33%). Half of NIV PARDS patients were subsequently intubated, with 25% mortality. They concluded that the PALICC definition discriminates children with ARDS based on their mortality risk than the Berlin definition.

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PALICC-2

The PALICC-2 was published in 2023 and was an update on the previous definition.[8] It kept the criteria for age group, timing of the onset, CXR, and origin of pulmonary edema the same as the previous PALICC definition. The most striking change is that the severity criteria for PARDS are applied after 4 hours of the initial diagnosis of PARDS. This more accurately depicted the final outcomes. The major change in this definition was the clubbing of the mild (OI >4) and moderate (OI >8) PARDS into one group, the mild/moderate PARDS group (OI >4 <16) and OI >16 continued to be severe PARDS. There was also a change in rounding off the OSI numbers to the nearest unit such that mild/moderate PARDS was represented by OSI >5 and <12. The other major change was in patients on a full-face interface of NIV (CPAP) or bilevel positive airway pressure (BiPAP) with CPAP greater than or equal to 5 cmH_2O should be considered as having PARDS if they meet timing, etiology/risk factor, and imaging criteria with oxygenation assessed using PaO_2/FiO_2 or SpO_2/FiO_2. Severe NIV PARDS is PF <100 or SF <150 while mild/moderate NIV PARDS is PF >100 or SF >150. The PALICC-2 also gave criteria for possible PARDS for children on nasal-only CPAP/BiPAP with a PEEP of >5 cmH_2O or on high-flow nasal cannula (HFNC) device with a flow of >1.5 L/kg/min or a flow of 30 L/min or above if they meet timing, etiology/risk factor, and imaging criteria with oxygenation status being PaO_2/FiO_2 ≤300 or SpO_2/FiO_2 ≤250. The criteria for CHD, CLD, and LV dysfunction remain the same except for the stratification as above.

The stratification timing was changed to 4 hours as those with milder disease would have stabilized with the initial management and this timing would accurately discriminate the severe PARDS in whom mortality is significantly high. The mild and moderate categories were clubbed as the observed mortality in the mild and moderate PARDS groups was very similar and significantly lower than in the severe group. Severity stratification was done even in NIV PARDS as it was observed that about 50% of severe NIV PARDS would go on to get intubated and the mortality may be as high as 25%. The possible PARDS was developed to sensitize the physicians to the possibility of PARDS diagnosis even when children are not on ventilation so that they may be monitored closely for worsening. There have been no published studies currently comparing the robustness of PALICC-2 with any other definitions.

One striking difference between how ARDS is defined and stratified in the adult population and in the pediatric population is that the adult population still uses the PF ratio in the Berlin definition, while the pediatric definition has moved over to the oxygenation index. Although the Berlin definition considers the applied PEEP, it still is a predominantly oxygenation-based index, while the PALICC definitions use OI, which includes mean airway pressure and hence it includes oxygenation as well as pulmonary mechanics in its definition to some extent. Indeed, studies have shown that a mere improvement in oxygenation in response to the application of PEEP does not imply that alveoli are well recruited as the improvement in oxygenation could be due to Henry's Law operating in the background or reduction in the blood flow across the intrapulmonary shunts.[9]

On the other hand, there are caveats attached to why mere improvement in lung compliance also may not be a suitable criterion. This is because if the applied pressure has resulted in only "tidal recruitment" where alveoli are open only during peak inspiration and collapse during expiration, the static compliance measured during such "tidal recruitment" would be significantly high without actual alveolar recruitment where alveoli should remain open during inspiration as well as expiration.[10] The best strategy should be a combination of the both oxygenation and lung mechanics (improvement of compliance, driving

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pressure) and also better removal of carbon dioxide.[11] Defining ARDS and classifying into appropriate severity categories are not only important for an appropriate therapeutic approach but also for research purposes where it is crucial not to include "ARDS mimics" in the studies which may skew the interpretation of the studies. As the use of high-flow humidified nasal canula oxygen therapy has seen a sharp increase due to its ease of use in resource-constraint settings, there are a group of researchers proposing removal of PEEP from the definition of ARDS.[12] This approach, however, may dilute the severity of illness among patients labeled as ARDS, as it would also capture patients with a better prognosis.[13] Criteria necessary for a definitive diagnosis of ARDS are increased pulmonary vascular permeability and diffuse alveolar disease (DAD). However, they are difficult to evaluate in actual clinical practice. Extravascular lung water can provide an idea about vascular permeability at the bedside, although how much pulmonary vascular permeability will be needed to predict DAD is still unclear.[14]

The European Society of Intensive Care Medicine (ESICM) guidelines have proposed hypoinflammatory and hyperinflammatory subphenotypes of ARDS based on 25 studies. The guidelines have cited the association of disease severity, treatment strategies, and outcomes with the subphenotypes (higher mortality in hyperinflammatory than in hypoinflammatory, higher mortality in recruitable than in nonrecruitable lungs, etc.).[15] There are several unanswered questions in this particular domain; however, this is an exciting premise to look forward to in future.

CONCLUSION

The evolving journey of ARDS definitions has arrived at the PALICC-2 framework currently. While it presents advantages for identifying pediatric cases and stratifying severity, the adoption of PALICC and PALICC-2 is still evident in the literature for standardization of care around the world, particularly in low- and middle-income group countries. We must remain committed to collaborative efforts using standard and uniform definitions to improve our understanding, refine diagnostic tools, and ultimately improve the outcomes for every child battling ARDS.

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During the preceding decade, there has been an augmented stream of knowledge, and useful technological advancements in the field of critical care medicine. For those who are treating critically ill children, it is extremely important to remain in tune and aware about these developments. At the same time, there have been variable challenges for the time and resource-constrained pediatricians to remain updated for the same. Thereby, there has been a need-felt to have a sourcebook with updated evidence-based literature and guidelines at one place. Here is this book which shall take care of the need as required. The topics are carefully selected keeping in mind the local context, settings, and the future of pediatric critical care. The section editors and the contributors are the mix of dedicated academicians with the desired experience, knowledge and wisdom who have worked hard for the set objectives. The book features the recent advances available in the field of pediatric critical care with the section for the recent society guidelines. We believe this book shall be one-point ready-desktop reference for one and all caring the sick children.

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