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## Nonadherence to Appropriate Tidal Volume and PEEP in Children with pARDS at a Single Center

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### Abstract

**Background:** Low tidal volume and adequate positive end-expiratory pressure (PEEP) are evidence-based approaches for pediatric acute respiratory distress syndrome (pARDS), however data are limited regarding their use since pARDS guidelines were revised in 2015.

**Objective:** To identify prevalence of, and factors associated with, nonadherence to appropriate tidal volume and PEEP in children with pARDS.

**Methods:** Retrospective cohort study of children 1 month-<18 years with pARDS who received invasive mechanical ventilation from 2016–2018 in a single pediatric intensive care unit (PICU).

**Results:** At 24 hours after meeting pARDS criteria, 48/86 (56%) patients received tidal volume 8 mL/kg of ideal body weight and 45/86 (52%) received appropriate PEEP, with 22/86 (26%) receiving both. Among patients > 2 years of age, a lower proportion of patients with overweight/obesity (9/25, 36%) had appropriate tidal volume vs. those in the normal or underweight category (16/22, 73%, p=0.02). When FIO<sub>2</sub> was ≥ 50%, PEEP was appropriate in 19/60 (32%) cases vs. 26/26 (100%) with FIO<sub>2</sub> <50% (p<0.0001). pARDS was documented in the progress note in 7/86 (8%) patients at 24 hours. Severity of pARDS, documentation in the progress note, and other clinical factors were not significantly associated with use of appropriate tidal volume and PEEP, however pARDS was documented more commonly in patients with severe pARDS.

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**Conclusions:** In a single PICU in the United States, children with pARDS did not receive appropriate tidal volume for ideal body weight nor PEEP. Targets for improving tidal volume and PEEP adherence may include overweight patients and those receiving FIO<sub>2</sub> 50%, respectively.

### Keywords

acute respiratory distress syndrome; pediatric; quality; positive end expiratory pressure; diagnosis; respiratory failure

## Introduction

Pediatric acute respiratory distress syndrome (pARDS) occurs in 3% of patients overall and 6% of those on mechanical ventilation<sup>1</sup> in the Pediatric Intensive Care Unit (PICU), and is associated with high in-hospital mortality (13–35%)<sup>1–4</sup> and new morbidity (23% of survivors)<sup>2</sup>. Low tidal volume ventilation and use of positive end expiratory pressure (PEEP) are key elements of ventilator management in ARDS and have been associated with decreased mortality in both adults and children<sup>4–6</sup>. Ventilator parameters in the first 24–72 hours after ARDS diagnosis have been shown to affect outcome<sup>4–5, 7</sup>, emphasizing the need for rapid recognition and evidence-based management.

Despite existing evidence, use of low tidal volume ventilation and PEEP appropriate for fraction of inspired oxygen (FIO<sub>2</sub>) deviate from recommendations 29–87% of the time in adults<sup>8–12</sup> and children<sup>4–5, 13–15</sup>. Reasons for these variations in care are incompletely described, but could include patient demographics<sup>12</sup>, intensive care unit or hospital organizational characteristics<sup>10, 15–16</sup>, usage of actual rather than ideal weight<sup>14–15, 17</sup>, delayed identification of ARDS<sup>9, 18</sup>, severity of disease<sup>5, 8, 10, 11–12, 18</sup>, provider perceptions and knowledge<sup>17–19</sup>, ventilator mode<sup>5</sup>, or other patient or illness characteristics<sup>11, 14–15, 17, 18–19</sup>.

New guidelines for diagnosis and management of pARDS were published in 2015<sup>20</sup>, resulting in an increased percentage of patients meeting criteria for pARDS earlier in their PICU course<sup>1</sup>. Furthermore, studies of adherence to evidence-based ventilator management in children included some or all of their patients in the context of prospective studies of pARDS<sup>4–5, 14</sup>, which may not reflect usual care. The objective of this study was to identify prevalence of, and factors associated with, nonadherence to 1) use of tidal volume 8 milliliters per kilogram (mL/kg) of ideal body weight and 2) PEEP appropriate for FIO<sub>2</sub> in children with pARDS in usual care in a tertiary PICU since publication of the 2015 guidelines.

## Methods

### Study population

Patient admissions 1 month to <18 years of age to the Wake Forest Brenner Children's Hospital PICU who received invasive mechanical ventilation during their stay, excluding those with cyanotic heart disease or receiving cardiac bypass, were identified over the time period January 1<sup>st</sup>, 2016 through December 31<sup>st</sup>, 2018. The study PICU has 11 beds with an adjacent intermediate care unit, located in a 193-bed Children's Hospital within a tertiary

care academic medical center designated as a level 1 adult and pediatric trauma center. At least one dedicated respiratory therapist is present in the PICU at all times. There is also a pediatric intensive care board-certified or board-eligible attending physician present in the PICU 24 hours per day along with resident providers, with no pediatric critical care fellows. The ventilator in use was the Servo-i (Getinge, Gothenburg, Sweden), and ventilator changes were made at the discretion of the care team with no formal mechanical ventilation protocol in place. No prepopulated fields for oxygenation index, oxygen saturation index, or ideal body weight were present in the electronic health record during the study period, nor were any decision support tools for tidal volume or peep titration.

## Study Design

This was a single center retrospective cohort study designed to identify factors associated with evidence-based management of pARDS. The exposure was first occurrence of pARDS during a PICU stay in a patient who received mechanical ventilation. The primary outcomes were a) use of tidal volume  $\leq 8$  mL/kg ideal body weight (actual body weight if  $<2$  years old) and b) use of minimum PEEP per fraction of inspired oxygen (FIO<sub>2</sub>) by the ARDSnet lower PEEP/higher FIO<sub>2</sub> table (Supplemental Content Table s1)<sup>6</sup> at 24 hours after the patient met criteria for ARDS. The secondary outcomes were parameters a) and b) at 72 hours after meeting criteria for ARDS. A pre-specified additional analysis was performed to evaluate presence of pARDS in the progress note at 24 and 72 hours, given that physician recognition of ARDS was perceived as the top barrier to initiation of lung-protective ventilation in a previous survey study<sup>18</sup>. Post-hoc evaluations of the progress note were also performed for presence of a) weight or obesity (if overweight or obese) and b) “respiratory failure” to evaluate further for possible indications of physician awareness of these conditions.

## Data Collection

Patient demographics, clinical features, and outcomes, including severity of illness by Pediatric Index of Mortality 3 (PIM 3)<sup>21</sup> and Pediatric Risk of Mortality 3 (PRISM III)<sup>22</sup>, were identified from local data previously collected and submitted to the Virtual Pediatric Systems (VPS, LLC) database. No additional data were provided by VPS, LLC; no endorsement or editorial restriction of the interpretation of these data or the opinions of the authors has been implied or stated.

Ventilator, blood gas, and vital sign data were obtained from the electronic medical record and time-linked. Patients were evaluated for inclusion if they received mechanical ventilation and met hypoxemia criteria for pARDS during their PICU stay. Patients meeting criteria while on non-invasive ventilation were required to be on conventional invasive mechanical ventilation by 24 hours so that the primary outcome could be assessed. Hypoxemia criteria for pARDS were assigned per 2015 PALICC guidelines<sup>20</sup>. Oxygenation index (OI) or oxygen saturation index (OSI) was used for invasively ventilated patients, with OI used preferentially in cases in which a PaO<sub>2</sub> was recorded. PaO<sub>2</sub>:FIO<sub>2</sub> (P:F) ratio or Saturation:FIO<sub>2</sub> (S:F) ratio was used for patients non-invasively ventilated with full face-mask continuous positive airway pressure (CPAP) or bi-level ventilation. Peak inspiratory pressure (PIP) was recorded as plateau pressure was not documented. Any values for OSI based on a saturation  $<88\%$  were reviewed to ensure that a sustained value rather than an

isolated value was used. All patient charts were also reviewed by one of the authors (AGW, ALB, or MCM) for additional pARDS criteria (acute insult within 7 days, respiratory failure not fully explained by cardiac failure or fluid overload, chest imaging findings). Patients on extracorporeal support or on ventilator modalities other than conventional ventilation (high frequency or airway pressure release) at 24 hours after meeting pARDS criteria were also excluded from the primary analysis, as tidal volume evaluation would be systematically different. Inhaled nitric oxide use was not evaluated in this study, as it is not recommended for routine use in pARDS<sup>20</sup>.

Body weight and height (length) were obtained from the medical record. Ideal body weight was determined using the McLaren method<sup>23–24</sup> and age and gender-specific Centers for Disease Control and Prevention (CDC) growth charts<sup>25</sup>. Ideal body weight was only calculated for children  $\geq 2$  years in this study given that ideal body weight calculations are less reliable in younger age groups<sup>26</sup> and CDC guidelines only define overweight/obesity categories in children  $\geq 2$  years<sup>27</sup>. For patients  $\geq 2$  years old, age, sex, height, and weight were used to categorize patients as having underweight, normal weight, overweight, and obesity according to Center for Disease Control (CDC) and Prevention guidelines<sup>27</sup>. Patients were classified based on BMI percentile for age and sex as follows: less than 5% underweight, 5% to less than 85% normal weight, 85% to less than 95% overweight, and greater than or equal to 95% obesity. Patients with obesity were further categorized into class 1 obesity (100–<120% of 95<sup>th</sup> percentile BMI) or class 2–3 obesity ( $\geq 120\%$  of 95<sup>th</sup> % BMI)<sup>28</sup>. For those classified in a category other than normal weight, predicted body weight was determined using the value for the closest percentile in the normal weight category for age/sex/height (i.e. 5<sup>th</sup> percentile if underweight and 85<sup>th</sup> % if overweight or obese).

Primary and secondary outcomes were collected from the electronic medical record as the point-in-time (steady state) tidal volume and PEEP at 24 and 72 hours after pARDS hypoxemia criteria were met, respectively. These time points were chosen for comparability with previous studies that have evaluated low tidal volume or PEEP use in acute lung injury or ARDS at or within the first 24<sup>4,9,14</sup> or 72<sup>5,13,15</sup> hours, as well as data indicating that ventilator settings in the first few days may affect outcome<sup>7</sup>. The 24-hour point was chosen as the primary outcome for direct comparability with the largest study of tidal volume adherence in pARDS prior to the 2015 guidelines<sup>14</sup>, as well as to allow time for recognition of pARDS and ventilator adjustment after hypoxemia criteria were met. Tidal volume was recorded as either the set (if in volume control mode) or measured (if in pressure control mode) value, then divided by either the measured (if  $<2$  years of age) or ideal body weight (if  $\geq 2$  years of age) to determine mL/kg. PEEP and FIO<sub>2</sub> were recorded at the predetermined time points (24 or 72 hours after meeting pARDS criteria) and designated as appropriate if PEEP was equal to or greater than the minimum recommended PEEP in the ARDSnet low PEEP/high FIO<sub>2</sub> table<sup>6</sup> (Supplemental Content Table s1). Any FIO<sub>2</sub> value in between values in the FIO<sub>2</sub>/PEEP table was rounded down to the nearest decile if  $\leq 5\%$  above and up if  $>5\%$  above (e.g. 45% FIO<sub>2</sub> was considered as 40%, but 48% FIO<sub>2</sub> was considered as 50%). The recommendations from the 2015 PALICC guidelines<sup>20</sup> of a) allowing permissive hypercapnia while maintaining pH between 7.15–7.30, excepting clinical circumstances such as elevated intracranial pressure or hemodynamic instability, and b) maintaining PEEP  $\geq 10$  cm H<sub>2</sub>O for patients with severe pARDS were also evaluated. Documentation of

pARDS was evaluated by review of the daily progress note for “acute respiratory distress syndrome”, “pARDS”, or “ARDS” on the calendar day of the primary and secondary outcomes (24 or 72 hours after meeting pARDS criteria) by one of the investigators (AGW, ALB, or MCM). Years of experience for each attending was calculated as the time from completion of fellowship to the first year of the study. Vasopressors were considered present if a continuous infusion of dopamine (dose 5 mcg/kg/min), epinephrine, norepinephrine, phenylephrine, or vasopressin (dose 0.0005 units/kg/min) was documented.

## Analyses

Continuous data were compared using the Student’s t-test if normally distributed and Wilcoxon rank-sum test if non-normally distributed. Proportions were compared using Pearson’s chi-square test or Fisher’s exact test, as appropriate. A two-tailed *p* value of <0.05 was considered statistically significant. Data were analyzed using SAS software version 9.4 (SAS Institute, Cary, NC). The Institutional Review Board of Wake Forest University School of Medicine approved this study (approval # IRB00059600).

## Results

At 24 hours after meeting pARDS criteria, 86 patient admissions in 80 unique patients were included in the primary analysis (Figure 1), representing 4.8% of total admissions and 15.6% of those with invasive ventilation. Demographic and clinical features of included patient admissions are in Table 1. Median length of PICU stay was 14.3 days (IQR 7.4–22.5) and 13 patients (15.1%) died in the PICU.

At 24 hours after meeting pARDS criteria, tidal volume 8 mL/kg of ideal body weight (measured body weight if <2 years of age) was present in 48/86 (56%) patients, and PEEP was appropriate for FIO<sub>2</sub> in 45/86 (52%) patients. In patients with severe pARDS, PEEP 10 was present in 9/18 (50%) cases at 24 hours. PICU mortality occurred in 4/48 (8.3%) patients with tidal volume 8 mL/kg vs. 9/38 (23.7%) with tidal volume >8 mL/kg (*p*=0.05) and 3/45 (6.7%) patients with appropriate PEEP vs 10/41 (24.4%) without (*p*=0.02). Median tidal volume was 7.7 mL/kg (IQR 6.5–9.0) and median PEEP was 8 (IQR 7–9). Both tidal volume and PEEP were appropriate in 22/86 (26%) cases. Tidal volume and PEEP status by patient characteristic at 24 hours is displayed in Table 2.

Peak inspiratory pressure was similar between patients with tidal volume 8 mL/kg (Median peak inspiratory pressure 24.2, IQR 20.1–29.1) vs tidal volume >8 mL/kg (Median peak inspiratory pressure 26.0, IQR 22.6–29.4, *p*=0.40) at 24 hours. Delta pressure (PIP-PEEP) was also similar [tidal volume 8 mL/kg: 17.6 (IQR 14–21), tidal volume >8 mL/kg: 17.7 (IQR 14–22), *p*=0.68]. In 84 patients with blood gas data available at 24 hours, median pH was 7.37 (IQR 7.31–7.42) and pCO<sub>2</sub> was 44.5 (IQR 37.0–52.5). pH was <7.15 in 3/84 (3.6%), between 7.15–7.30 in 13/84 (15.5%), and >7.30 in 68/84 (81%), while pCO<sub>2</sub> was <60 mm Hg in 74/84 (88%). In patients with tidal volume nonadherence, 0/38 (0%) had pH<7.15, 10/38 (26.3%) had pH between 7.15–7.30, and 28/38 (74%) had pH>7.30. Median SpO<sub>2</sub> at 24 hours was 95% (IQR 92–97) and PaO<sub>2</sub> (n=50) was 74 mm Hg (IQR 62–102). SpO<sub>2</sub> was <92% in 19/86 (22%), 92–97% in 56/86 (65%), and >97% in 11/86 (13%) patients; among those with PEEP 10 cm H<sub>2</sub>O (n=18), SpO<sub>2</sub> was <88% in 2/18 (11%),

88–92% in 7/18 (39%), and >92% in 9/18 (50%). There were no significant differences in tidal volume or PEEP adherence at 24 hours by pARDS hypoxemia criterion used, study year, oxygenation data, or use of vasopressor support; however, pCO<sub>2</sub> was significantly higher and proportion with pH between 7.15–7.30 was significantly lower in patients with tidal volume  $\geq 8$  mL/kg, while PIM3 risk of mortality was significantly lower in patients with appropriate PEEP at 24 hours. (Supplemental Content Table s2) In patients with head trauma and intracranial pressure monitoring in place at 24 hours, 5/6 (83%) had appropriate tidal volume and 3/6 (50%) had appropriate PEEP. pH was >7.30 and pCO<sub>2</sub> was <40 in 4/5 (80%) of head trauma patients with tidal volume adherence. Among patients declared brain dead by 72 hours, 2/5 (40%) had appropriate tidal volume and 1/5 (20%) had appropriate PEEP at 24 hours.

Among patients for whom an ideal body weight and weight category was assigned (2 years of age, n=47), a lower proportion of patients with overweight/obesity (9/25, 36%) had a tidal volume  $\geq 8$  mL/kg of ideal body weight vs. those with normal or underweight category (16/22, 73%, p=0.02). Tidal volume per kg of ideal body weight was highest for the patients with Class 2–3 obesity (n=8, median 9.6 mL/kg, IQR 7.8–10.0), followed by Class 1 obesity (n=12, 9.1 mL/kg, IQR 7.5–10.1), and overweight patients (n=5, 8.5 mL/kg, IQR 7.7–8.7), as shown in Figure 2. When tidal volume was evaluated based on measured body weight for all patients, median tidal volume was 7.1 mL/kg (IQR 6.3–8.1) and 59/86 (69%) patients had tidal volume  $\geq 8$  mL/kg, with 11 patients (13%) appearing to have tidal volume  $\geq 8$  mL/kg when this was not the case by ideal body weight. Age was no longer significantly associated with use of appropriate tidal volume  $\geq 8$  mL/kg when actual body weight was used {tidal volume  $\geq 8$  mL/kg: 1–23 months 23/39 (59%), 2–5 years 13/16 (81%), 6–12 years 14/19 (74%), 13–<18 years 9/12 (75%), p=0.34}.

PEEP used for each FIO<sub>2</sub> value is displayed in Figure 3. Median PIP for patients with appropriate PEEP was 25.7 (IQR 22.0–29.0) vs. 25.0 (IQR 22.7–30.0) in patients with insufficient PEEP (p=0.72). Among those observations with FIO<sub>2</sub>  $\geq 50\%$ , PEEP was appropriate for FIO<sub>2</sub> in 19/60 (32%) cases, vs 26/26 (100%) when FIO<sub>2</sub> was <50% (p<0.0001). In patients with FIO<sub>2</sub>  $\geq 80\%$ , 0/15 (0%) had an appropriate PEEP.

At 72 hours after meeting ARDS criteria, 50/86 (58%) patients continued to meet study criteria (Figure 1) and were included in the secondary analysis. Tidal volume  $\geq 8$  mL/kg was present in 29/50 (58%) cases and PEEP was appropriate for FIO<sub>2</sub> in 34/50 (68%) cases, with both parameters met in 19/50 (38%) cases. In patients with severe pARDS, PEEP  $\geq 10$  was present in 5/7 (71%) patients at 72 hours. Documentation in the progress note was poor for both pARDS (7/86=8% of progress notes at 24 hours, 6/50=12% at 72 hours) and overweight/obesity (3/25=12% at 24 hours), while “respiratory failure” was often documented (70/86=89% at 24 hours). Documentation occurred in a higher proportion of patients with severe pARDS at both 24 (severe 4/18, 22% vs mild or moderate 3/68, 4%, p=0.01) and 72 hours (severe 4/7, 57% vs mild or moderate 2/43, 5%, p=0.002). Characteristics of patients with tidal volume  $\geq 8$  mL/kg or PEEP appropriate for FIO<sub>2</sub> at 72 hours are displayed in Supplemental Content Table s3.

## Discussion

In this single center retrospective study evaluating evidence-based ventilator management 24 hours after criteria were met for pARDS, just over half of patient admissions had tidal volume  $\geq 8$  ml/kg ideal body weight (56%) or PEEP appropriate for FIO<sub>2</sub> (52%), with a minority (26%) having both. The percentage of patients achieving these parameters were only marginally better at 72 hours for tidal volume (58%), PEEP (68%), and both (38%).

The incidence of pARDS, mortality, and proportion of patients with tidal volume and PEEP adherence under usual care in this single tertiary PICU were similar to previous studies<sup>1,4-5,14</sup>, suggesting that these findings may be comparable in many PICUs, that nonadherence persists since publication of the 2015 PALICC guidelines<sup>20</sup>, and that any Hawthorne effect on adherence in the context of previous prospective studies was minimal. Furthermore, the additional data points collected in this study such as severity of illness, vasopressor use, head trauma, documentation in progress notes, and goal pH and SpO<sub>2</sub> ranges may provide further hypotheses to guide quality improvement efforts.

Although the PALICC guidelines identify 40% more children as having ARDS at a median of 12.8 hours sooner than prior criteria<sup>1</sup>, adherence to tidal volume and PEEP goals were not significantly different by severity of ARDS, hypoxemia criterion, duration since meeting criteria (24 vs 72 hours), or documentation of ARDS in the progress note (although documentation was only present in 8% of patients at 24 hours) in this study. However, the small number of patients (n=7) with severe ARDS at 72 hours had both the highest adherence to tidal volume  $\geq 8$  mL/kg (86%) and the highest proportion with ARDS documented in the progress note (57%). The lack of association in this study between pARDS severity and ventilator management at 24 hours was similar to one prior study<sup>14</sup>, however in another study<sup>5</sup> severe pARDS was actually associated with worse adherence to tidal volume ventilation and PEEP goals, suggesting that adherence may be hampered by actual or perceived patient instability.

Provider management of tidal volume and PEEP may relate to multiple aspects of organ system dysfunction in a critically ill child besides lung disease, such as neurologic (impact of pH/PaCO<sub>2</sub> on cerebral bloodflow) or cardiovascular (impact of pH or mean airway pressure on cardiac output) considerations. Patients with PEEP non-adherence at 24 hours had significantly higher PIM3 risk of mortality, suggesting that overall severity of illness may have been related to PEEP titration. Patients with head trauma and intracranial pressure monitoring actually had a relatively high adherence (5/6, 83%) to tidal volume  $\geq 8$  ml/kg in this study, however the pCO<sub>2</sub> remained  $<40$  in the majority (80%) of head trauma patients with tidal volume adherence, suggesting that permissive hypercapnia was not necessary. In patients on vasopressor infusions, there was lower observed adherence to both tidal volume (42% adherence in patients on vasopressors vs 62% in those not on vasopressors) and PEEP (42% adherence on vasopressors vs 57% not) at 24 hours, but these results were not statistically significant. These findings could indicate concerns about hypercapnia and acidosis with low tidal volume use, consistent with a survey of providers for adults with ARDS<sup>18</sup>. Among those with tidal volume non-adherence there was a significantly higher percentage of patients with pH between 7.15–7.30 (26% vs 6% of those with tidal volume

adherence), with a significantly lower pCO<sub>2</sub> (median 40 vs. 48 in those with tidal volume adherence). However, the pH was similar and within normal parameters in patients on vasopressors regardless of tidal volume or PEEP adherence, suggesting that cardiovascular stability may not have been compromised by lowering tidal volume or increasing PEEP even on vasopressors. Finally, in study patients with brain death by 72 hours after meeting ARDS hypoxemia criteria (n=5), only 40% met tidal volume goal and 20% met PEEP goal at 24 hours, suggesting that de-prioritization of lung protection may have taken in place in patients with non-survivable neurologic injury.

The strongest association with use of tidal volume 8 ml/kg in our study was weight category, suggesting that practitioners may not be routinely recognizing or using ideal body weight for ventilator management, consistent with previous studies in children with ARDS<sup>5,14</sup>. The poor documentation of overweight/obesity (3/25, 12%) in the progress notes is consistent with previous studies reporting weight status documentation in only 8.3–26% pediatric inpatients with obesity<sup>29–30</sup>. Furthermore, there was a higher observed tidal volume adherence (though not statistically significant) in patients on a pressure control mode of ventilation, suggesting that when actual body weight was used instead of ideal, a volume control setting (presumably used to attempt to actively maintain appropriate tidal volumes) was actually more likely to deliver potentially injurious tidal volumes. The association between age and lower tidal volume use disappeared when actual body weight was used, with a particular difference in patients 6–18 years old. These findings suggest that increasing provider awareness of overweight/obesity and ideal body weight, especially in children 6 years old, may be an attractive target to improve use of lower tidal volume ventilation.

The strengths of this study include the rigorous approach to identifying cases of pARDS using medical record data combined with chart review. Many features of care were able to be extracted that have been rarely evaluated in other studies, including documentation of pARDS or weight/obesity status in the progress note, tracheostomy status, pH, severity of illness by both PIM3 and PRISM III, vasopressor infusions, attending years of experience, and head trauma. Furthermore, since these data were collected under usual care, any potential impact of the Hawthorne effect in the setting of a prospective study of pARDS was not present.

The primary weakness of this study is its single center nature, however, the similarity of the population characteristics as well as the use of tidal volume and PEEP to other reports<sup>1, 4–5, 14</sup> suggest that associations reported here may be generalizable. Nonetheless, given the relatively low numbers from a single center, these results can primarily be considered as hypothesis-generating to guide future quality improvement investigations, especially with respect to documentation in the daily progress note since this may not be reflective of care team awareness of pARDS. Additionally, although the PALICC guidelines recommend tidal volume use 8 mL/kg, the association between tidal volume and outcome in children with pARDS<sup>31–33</sup>, as well as the appropriate calculation of ideal body weight in children<sup>24</sup>, are sources of substantial inconsistency in the literature, and it is unclear what effect this ambiguity may have had on provider decision-making especially when peak inspiratory pressure was not high. Similarly, the ARDSnet tables for PEEP and FIO<sub>2</sub> have been available since their publication in 2000<sup>6</sup>, but these PEEP parameters are not



explicitly recommended in the pARDS guidelines and the strongest data supporting their use in children were published during the last year of the data collected in this study<sup>4</sup>. The study was designed to evaluate adherence, and there was lower observed severity of illness in patients with tidal volume and PEEP adherence, therefore the lower mortality in these patients should be interpreted with caution. The outcomes were also evaluated as point-in-time rather than continuous or average values for tidal volume and PEEP, which facilitated comparison with some previous studies<sup>9,14</sup> allowed time for clinicians to recognize pARDS and titrate settings, and corresponded with other data points such as progress note documentation, but may have not have reflected true values for these parameters if settings were changed frequently. A ventilator protocol was not used in this study, although use of such protocols has not been quantified in previous studies of lung-protective ventilation in pARDS<sup>5,14</sup>, and their utility is unknown. Finally, while alternate ventilator modalities and use of inhaled nitric oxide are not routinely recommended in pARDS<sup>20</sup> and were not evaluated in this study, both can be considered in certain clinical situations and their use may influence variations in provider decisions regarding escalation in tidal volume and PEEP. The relatively low number of patients on alternate ventilator modalities at 24 hours (n=4) may reflect different practice patterns than some other PICUs.

Overall, it appears that providers in this study had a usual comfort range of ventilator parameters and set the tidal volume and PEEP within those ranges, around 7–8 mL/kg (IQR 6.3–8.1 based on actual body weight) and PEEP 5–10, but were not responsive to patient factors that should have prompted adjustment, especially overweight/obesity and escalating FIO<sub>2</sub>. There also appeared to be a usual comfort range of pH (>7.30), pCO<sub>2</sub> (<60), and SpO<sub>2</sub> (>92%) that providers often accepted without adjusting settings when pARDS was present. Additionally, providers did not routinely document when a patient had pARDS; documentation was slightly improved in the presence of severe pARDS. Progress notes in this study included “respiratory failure” in the note much more frequently than “pARDS”, perhaps because this phrase is considered sufficient to justify critical care billing<sup>34</sup> and thus becomes routine unless more severe hypoxemia prompts pARDS recognition. Patients with tidal volume and PEEP nonadherence generally had higher observed severity of illness scores and lower pH, suggesting that overall critical status led to decreased recognition or prioritization of tidal volume and PEEP adherence, not necessarily attributable to elevated PIP, severe acidosis with pH <7.15, hemodynamic instability, or head trauma. We hypothesize that the system of care in place, specifically the lack of prepopulated fields to aid the provider in identifying pARDS hypoxemia criteria or ideal body weight, as well as lack of decision tools to streamline evidence-based management (such as PEEP/FIO<sub>2</sub> tables) could be an important reason for the observed tidal volume and PEEP nonadherence. Integration of such tools, streamlined into workflow either in the electronic medical record or at the bedside, could ease cognitive burden on providers especially in the setting of more critically unstable patients and improve evidence-based management of pARDS.

## Conclusions

In a single PICU in the United States, children with pARDS did not receive appropriate tidal volume for ideal body weight nor PEEP. Interventions to increase the use of appropriate tidal volume may include improving provider awareness and documentation of pARDS and

ideal body weight, while interventions for improving the use of appropriate PEEP may target patients receiving FIO<sub>2</sub> 50%.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Data Availability Statement:

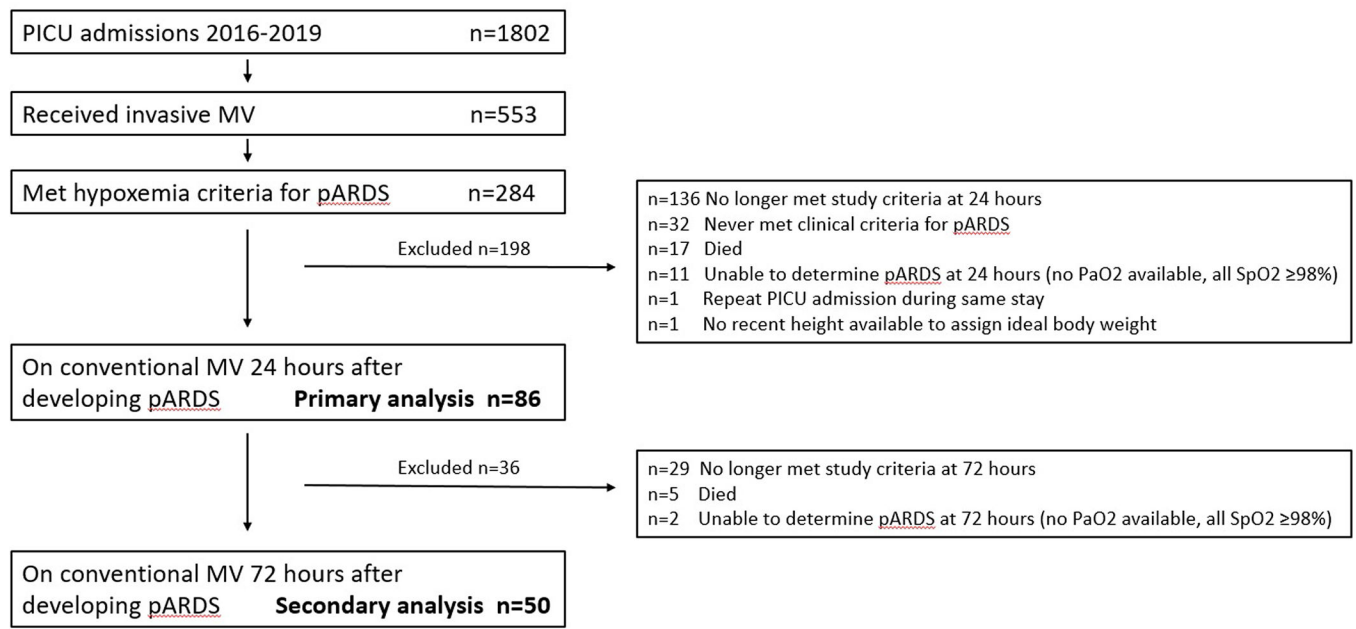
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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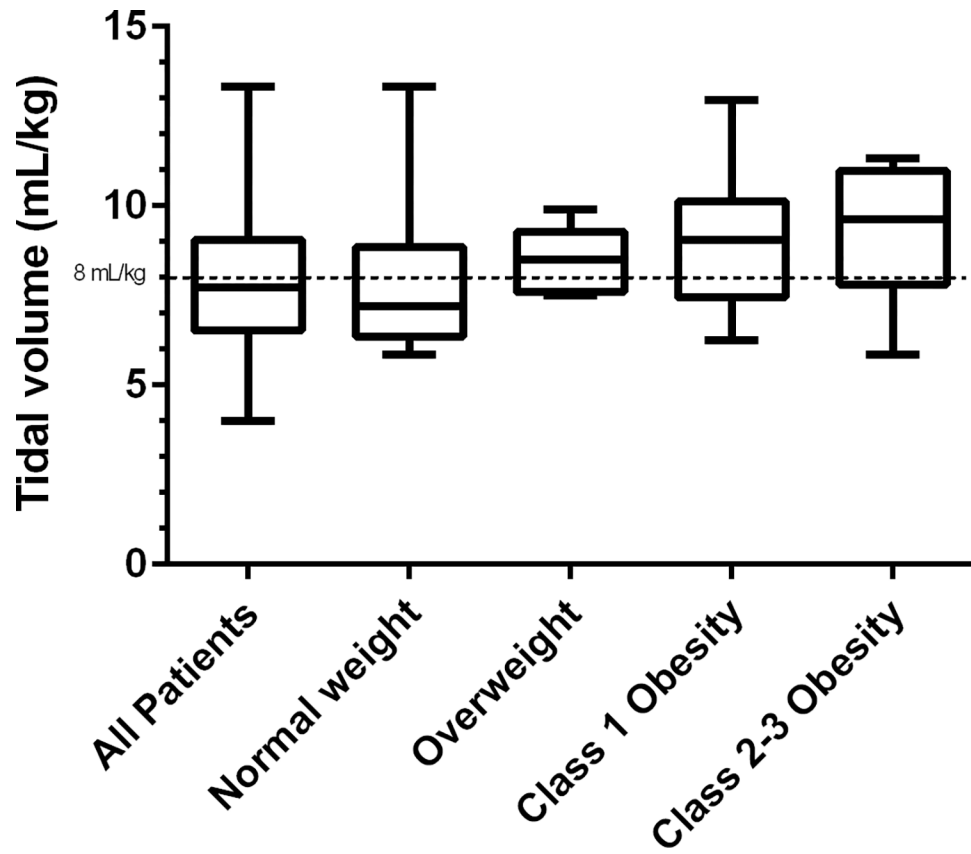
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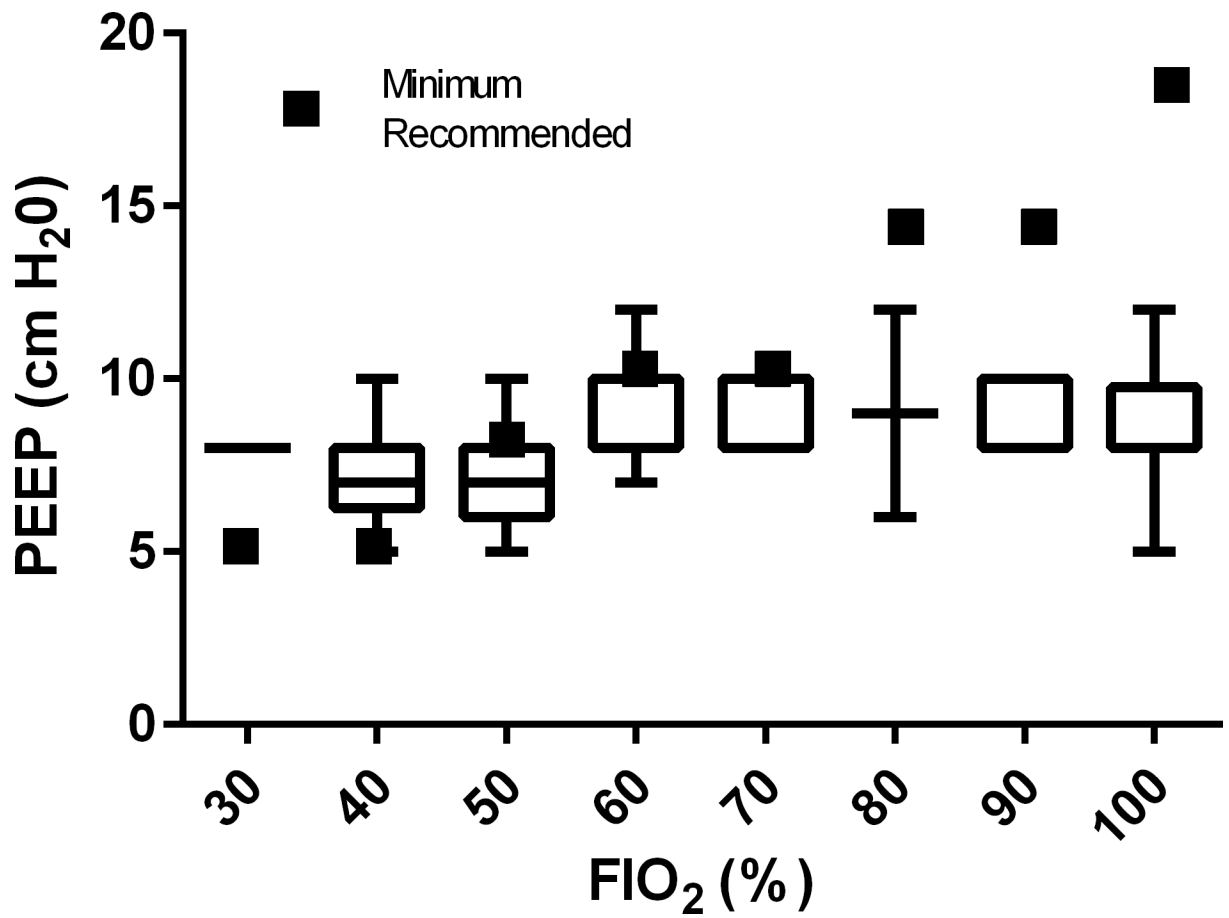
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**Figure 1:** Study flow diagram. MV: Mechanical Ventilation. pARDS: pediatric acute respiratory distress syndrome. PICU: pediatric intensive care unit. Among those (n=136) who did not meet study criteria at 24 hours: Conventional ventilation without ARDS n=79, extubated or off of positive pressure ventilation by tracheostomy n=32, transferred/discharged/not in PICU n=15, never intubated n=4, other ventilator modality (airway pressure release or high frequency) n=4, on extracorporeal support n=2.



**Figure 2:** Tidal volume (mL/kg of ideal weight if  $\geq 2$  years of age, actual weight if  $<2$  years) by weight category. All patients: n=86; Normal weight: n=18; Overweight n=5; Class 1 Obesity: n=12; Class 2–3 Obesity n=18



**Figure 3:** PEEP (cm H<sub>2</sub>O) by FIO<sub>2</sub> at 24 hours after meeting ARDS hypoxemia criteria. All patients: n=86; FIO<sub>2</sub> 30%: n=2, FIO<sub>2</sub> 40%: n=24, FIO<sub>2</sub> 50%: n=27, FIO<sub>2</sub> 60%: n=13, FIO<sub>2</sub> 70%: n=5, FIO<sub>2</sub> 80%: n=2, FIO<sub>2</sub> 90%: n=5, FIO<sub>2</sub> 100%: n=8.

**Table 1 –**

Characteristics of included patient admissions

Category	Total n=86
Age months, median(IQR)	33.5 (7.0–103.0)
Age category, n(%)	
1 month–<2 years	39 (45%)
2–5 years	16 (19%)
6–12 years	19 (22%)
13–<18 years	12 (14%)
Gender=male, n(%)	46 (53%)
Race, n(%)	
White	43 (50%)
Black or African American	20 (23%)
Other/Mixed/Unspecified	16 (19%)
Hispanic or Latino	7 (8%)
Weight category, n(%) (among n=47 2 yrs old)	
Normal/underweight	22 (47%)
Overweight	5 (11%)
Obese	20 (43%)
Tracheostomy tube in place	11 (13%)
Risk of mortality (probability of death) on admission, mean (SD)	
PIM 3	15.3 (27.3)
PRISM-III	16.6 (28.5)
Primary Cause of pARDS, n(%)	
Respiratory	49 (57%)
Systemic	37 (43%)
Initial pARDS hypoxia criterion met n(%)	
Invasive Ventilation	
Oxygenation Saturation Index (OSI)	55 (64%)
Oxygenation Index (OI)	28 (33%)
Non-invasive Ventilation	
PaO2: FIO2 (P:F) ratio	2 (2%)
Saturation: FIO2 (S:F) ratio	1 (1%)
Initial pARDS Severity	
Mild	36 (42%)
Moderate	19 (22%)
Severe	28 (33%)



Category	Total n=86
Not applicable (non-invasive ventilation)	3 (3%)
Year of Admission	
2016	40 (47)
2017	19 (22)
2018	27 (31)

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**Table 2 –**

Tidal volume and PEEP at 24 hours

Characteristic Total n=86	TV 8 mL/kg	p	PEEP appropriate for FIO <sub>2</sub>	p
<b>Age group</b>				
1 month-<2 years	23/39 (59%)	<b>0.04</b>	17/39 (44%)	0.15
2–5 years	13/16 (81%)		7/16 (44%)	
6–12 years	7/19 (37%)		14/19 (74%)	
13–<18 years	5/12 (42%)		7/12 (58%)	
<b>Gender</b>				
Female	24/40 (60%)	0.47	20/40 (50%)	0.69
Male	24/46 (52%)		25/46 (47%)	
<b>Race</b>				
White	21/43 (49%)	0.64	21/43 (49%)	0.74
Black or African American	13/20 (65%)		10/20 (50%)	
Other/Mixed/Unspecified	10/16 (63%)		9/16 (56%)	
Hispanic or Latino	4/7 (57%)		5/7 (71%)	
<b>Weight category ( 2 years old, n=47)</b>				
Normal/underweight	16/22 (73%)	<b>0.046</b>	13/22 (59%)	0.76
Overweight	2/5 (40%)		4/5 (80%)	
Obese	7/20 (35%)		11/20 (55%)	
<b>Tracheostomy tube present</b>				
No	40/75 (53%)	0.33	40/75 (53%)	0.75
Yes	8/11 (73%)		5/11 (45%)	
<b>pARDS cause</b>				
Respiratory	30/49 (61%)	0.25	26/49 (53%)	0.88
Systemic	18/37 (49%)		19/37 (51%)	
<b>pARDS severity</b>				
<u>Initial</u> Mild	19/36 (53%)	0.55	25/43 (58%)	0.49
Moderate	11/19 (58%)		13/25 (52%)	
Severe	15/28 (54%)		10/18 (56%)	
N/A (non-invasive vent)	3/3 (100%)		3/3 (100%)	
<u>24 hours</u> Mild	25/43 (58%)	0.89	28/43 (65%)	0.35
Moderate	13/25 (52%)		11/25 (44%)	
Severe	10/18 (56%)		6/18 (33%)	
<b>Ventilator mode</b>				
Pressure regulated volume control	38/73 (52%)	0.08	40/73 (55%)	0.11
Pressure control/pressure support	9/11 (82%)		3/11 (27%)	
CPAP with pressure or volume support	1/2 (50%)		2/2 (100%)	

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Characteristic Total n=86	TV 8 mL/kg	p	PEEP appropriate for FIO <sub>2</sub>	p
pARDS in progress note at 24 hours				
No	45/79 (57%)	0.69	40/79 (51%)	0.44
Yes	3/7 (43%)		5/7 (71%)	

Notes: All were on conventional mechanical ventilation using Servo-i (Maquet corporation) in synchronized intermittent mechanical ventilation (SIMV) setting. Bold indicates p<0.05.

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