Dynamic Airway Driving Pressure and Outcomes in Children With Acute Hypoxemic Respiratory Failure

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BACKGROUND: Limited adult data suggest that airway driving pressure might better reflect the potential risk for lung injury than tidal volume based on ideal body weight, and the parameter correlates with mortality in ARDS. There is a lack of data about the effect of driving pressure on mortality in pediatric ARDS. This study aimed to evaluate the effect of driving pressure on morbidity and mortality of children with acute hypoxemic respiratory failure. METHODS: This retrospective cohort study was performed in a tertiary level pediatric ICU. Children who received invasive mechanical ventilation for acute hypoxemic respiratory failure (defined as P_{aO_2}/F_{IO_2} < 300 within 24 h after intubation), in a 2-y period were included. The cohort was divided into 2 groups based on the highest dynamic driving pressure (ΔP, calculated as the difference between peak inspiratory pressure and PEEP) in the first 24 h, with a cutoff value of 15 cm H_2O. RESULTS: Of the 380 children who were mechanically ventilated during the study period, 101 children who met eligibility criteria were enrolled. Common diagnoses were pneumonia (*n* = 51), severe sepsis (*n* = 24), severe dengue (*n* = 10), and aspiration pneumonia (*n* = 7). In comparison to the group with high ΔP (ie, ≥ 15 cm H_2O), children in the group with low ΔP (ie, < 15 cm H_2O) had significantly lower median (interquartile range) duration of ventilation (5 [4–6] d vs 8 [6–11] d, *P* < .001], ICU length of stay (6 [5–8] d vs 12 [8–15] d, *P* < .001], and more ventilator-free days at day 28 (23 [20–24] vs 17 [0–22] d, *P* < .001). Logistic regression analysis also suggested driving pressure as an independent predictor of morbidity after adjusting for confounding variables. However, there was no statistically significant difference in mortality between the 2 groups (17% in low ΔP vs 24% in high ΔP, *P* = .38). Subgroup analysis of 65 subjects who fulfilled ARDS criteria yielded similar results with respect to mortality and morbidity. CONCLUSIONS: Below a threshold of 15 cm H_2O, ΔP was associated with significantly decreased morbidity in children with acute hypoxemic respiratory failure. *Key words: driving pressure; mechanical ventilation; ventilator induced lung injury; ARDS; outcome.*
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Introduction

Mechanical ventilation can induce and exacerbate lung injury, though it is one of the main supportive therapies for children with respiratory failure.[1] Volutrauma from large tidal volumes contributes to ventilator-induced lung injury partly by the dynamic strain imposed on the lungs.[2] Hence, the use of lung-protective tidal volume, set according to the ideal body weight, is a key part of the current lung-protective ventilation strategy in ARDS.[3] However, it is believed that ventilator-induced lung injury is not always prevented by reducing the tidal volume.[4] As the lung available for ventilation is significantly and nonuniformly reduced, a

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similar tidal volume based on ideal body weight can generate varying lung stress in different patients with ARDS.

Airway driving pressure is measured as the airway pressure changes from PEEP to end-inspiratory plateau pressure and is equivalent to the ratio between the tidal volume and compliance of the respiratory system. Driving pressure may provide a better estimate of lung stress because the applied tidal volume is related to the compliance of respiratory system.[5] Transpulmonary pressure has been used to represent global lung stress, but it requires measurement of esophageal pressure, which is neither widely available nor commonly used in children. Driving pressure is easy to calculate at the bedside and correlates directly with transpulmonary pressure in patients with normal chest wall compliance.

Amato et al[6] reanalyzed data from previous studies and were the first to show that driving pressure had a relationship with mortality in adults with ARDS. Though similar findings were reproduced later in a few other studies, the exact safe threshold of driving pressures is currently unclear. Bugedo et al[7] suggested a cutoff value of 15 cm H_2O as a safe threshold for driving pressure in adults, which is the same value found in the study by Amato et al.[6] The driving pressure threshold predicting mortality found in other studies varied from 14 to 18 cm H_2O.[8-10]

Pediatric data regarding the association of mortality with driving pressure are scarce. The objective of this study was to evaluate the association of driving pressure and outcomes in children with acute hypoxemic respiratory failure who require invasive mechanical ventilation.

QUICK LOOK

Current knowledge

Airway driving pressure correlates with mortality in adults with ARDS. The commonly proposed safety threshold of driving pressure in adults is 15 cm H_2O.

What this paper contributes to our knowledge

In children with acute hypoxemic respiratory failure, dynamic driving pressure with a safety cutoff of 15 cm H_2O was associated with lower morbidity as evidenced by shorter duration of ventilation and shorter ICU and hospital length of stay. However, there was no significant difference in mortality between the 2 groups, categorized using 15 cm H_2O as the cutoff value of driving pressure.

Methods

Eligibility Criteria and Enrollment

This was a retrospective cohort study done in the pediatric ICU of a tertiary care multi-speciality hospital in North India. Medical records of all consecutive children age 1 month to 15 y admitted to the pediatric ICU with a diagnosis of acute hypoxemic respiratory failure between July 1, 2016, and June 30, 2018, were screened for enrollment. Acute hypoxemic respiratory failure was defined as acute-onset illness (< 7 d) with at least one P_{aO_2}/F_{IO_2} value < 300 within 24 h after intubation.[11] We excluded children with congenital and acquired heart diseases, neuromuscular diseases, or primary immunodeficiency. Children with these diseases were excluded because they can independently affect the outcome parameters like duration of ventilation.[12] We also excluded patients with incomplete medical records. Approval from the institutional ethics committee was obtained. The need for informed consent was waived due to the retrospective nature of the study.

Usual Unit Protocol

Following the usual unit protocol for ventilation in children with acute hypoxemic respiratory failure, all patients were intubated using a cuffed endotracheal tube with the intention to minimize air leak across the tube. The pressure-regulated volume control mode with decelerating flow pattern was used as the default initial mode of ventilation in all children with acute hypoxemic respiratory failure.

A lung-protective ventilation strategy (5–6 mL/kg tidal volume, based on ideal body weight) and adequate PEEP (≥ 5 cm H_2O) was initiated in all subjects with hypoxemic respiratory failure. Ideal body weight was calculated using McLaren method, which compares weight and height in relation to a child's age using standard growth charts.[13] Stepwise increases of PEEP were performed to allow a reduction of F_{IO_2}, targeting an S_{pO_2} value of 88–92%. All children were kept under deep sedation during the first 24 h after intubation, and neuromuscular blocker infusion was used in those with $P_{aO_2}/F_{IO_2} < 150$. Use of high-frequency oscillatory ventilation or extracorporeal membrane oxygenation was considered when conventional ventilation failed (defined as persistently elevated peak inspiratory pressure [PIP; ie, ≥ 35 cm H_2O], hypercarbia [$P_{aCO_2} \geq 80$ mm Hg], or refractory hypoxemia [inability to wean $F_{IO_2} \leq 0.60$ despite increasing PEEP]). Driving pressure was not used as an index to titrate ventilation during the study period.

An evidence-based institutional protocol for weaning was used. The process of weaning was initiated when there was an improvement or resolution of the underlying disease and predefined criteria were met. These included alert mental status, effective cough and gag reflexes, spontaneous respiratory efforts, arterial pH 7.32–7.47, $P_{aO_2} > 60$ mm Hg on $F_{IO_2} \leq 0.40$, PEEP ≤ 7 cm H_2O, $P_{aCO_2} < 50$ mm Hg, and absence of escalation of inotropic support in the

preceding 24 h. When subjects fulfilled these criteria, they underwent a daily extubation readiness test using a 2-h trial of CPAP with minimal pressure support, adjusted for the endotracheal tube size (3–3.5 mm = pressure support of 10 cm H_2O; 4–4.5 mm = pressure support of 8 cm H_2O; > 5 mm = pressure support of 6 cm H_2O). Subjects with a breathing frequency higher than the 90th percentile for age, signs of increased work of breathing, tachycardia higher than the 90th percentile for age, $S_{pO_2} < 90\%$, $P_{aCO_2} > 50$ mm Hg or an increase of > 10 mm Hg from baseline, arterial pH < 7.3, or change in mental status at any time during the 2-h period are considered to have failed the extubation readiness test. Extubation was done when the extubation readiness test was successful.

Data Collection

Data were recorded on a study-specific clinical record form that included demographics, diagnosis, Pediatric Risk of Mortality in first 12 h (PRISM-12) score, ventilator settings, and variables of lung mechanics and oxygenation. As per routine practice in our unit, ventilator settings and variables of lung mechanics are recorded in the nursing observation charts. During the first 24 h of ventilation, ventilatory pressures are recorded every 6 h during periods of passive breathing under sedation or neuromuscular blockade by trained nurses, who identify absence of spontaneous breathing by matching the set breathing frequency with the observed frequency. The first set of values of these parameters are recorded at least 1 h after intubation. In this study, the first 4 sets of the ventilatory parameters, variables of gas exchange, and lung mechanics collected every 6 h were noted in the clinical record form. Of the 4 set of values recorded, the "worst" value for the day (eg, the highest tidal volume, the highest driving pressure) was considered for analysis purposes. Tidal volume was expressed in mL/kg ideal body weight. PIP was taken as a surrogate of plateau pressure as this cohort was ventilated with decelerating flow. Hence, the difference between PIP and PEEP was termed dynamic driving pressure (ΔP).[14]

Occurrence of organ dysfunction at 24 h (defined per diagnostic criteria given by the 2002 International Pediatric Sepsis Consensus Conference), cumulative fluid balance, and use of adjunct therapies of ARDS were also noted.[15] Enrolled children were also screened for fulfilment of ARDS criteria as per the 2015 Pediatric Acute Lung Injury Consensus Conference (PALICC).[16]

Clinical Methods

Enrolled children were separated into 2 groups based on a dynamic driving pressure cutoff of 15 cm H_2O, as proposed by Bugedo et al[7] (low driving pressure: $\Delta P < 15$ cm H_2O; high driving pressure: $\Delta P \geq 15$ cm H_2O). Outcome variables including duration of ventilation, pediatric ICU length of stay, hospital length of stay, ventilator-free days at day 28, and in-hospital mortality were recorded and compared between the 2 groups. Subjects were also grouped on the basis of morbidity parameters to identify morbidity predictors using regression models to account for confounding variables. For analysis purposes, significant morbidity was considered a dichotomous variable, and subjects with significant morbidity were defined as those who had both duration of ventilation > 7 d and ICU length of stay > 10 d or those who died. This definition was based on the median duration of ventilation (ie, 7 d) and ICU length of stay (ie, 10 d) in pediatric subjects with ARDS reported from 2 studies.[17,18]

Statistical Analysis

Baseline demographic features and descriptive clinical data were summarized using means ± SD or medians with interquartile ranges (IQR) for continuous variables and percentages for categorical variables. For normally distributed quantitative data, the *t* test was applied for the comparison of 2 groups. For skewed data or ordered categorical data, non-parametric Mann-Whitney *U* test and the Kruskal-Wallis test were used. For categorical data, comparisons were made with the Pearson chi-square test or the Fisher exact test as appropriate. The minimum threshold value of driving pressure for mortality was estimated with receiver operating characteristic curves by stepwise analysis using increasing values of driving pressure. Univariate analysis was performed to identify predictors of morbidity and mortality. Factors proven to have association with mortality and morbidity in various previous studies were chosen as variables for univariate analysis.[19-21] Appropriate cutoff values for categorizing different variables in the regression model were determined using receiver operating characteristic curves. Factors with $P < .05$ were considered significant and were subjected to multivariable logistic regression. Adjusted odds ratio were calculated for factors that were significant after multivariate analysis. Analysis was performed SPSS 22.0 (IBM, Armonk, New York).

Results

Of the 380 children who were mechanically ventilated during the study period, 161 children met the criteria for acute hypoxemic respiratory failure. Sixty patients were excluded due to cardiac disease ($n = 36$), neuromuscular disease ($n = 19$), primary immunodeficiency ($n = 3$), or incomplete medical records ($n = 2$). The remaining 101 children were enrolled in the study and analyzed.

The median (IQR) age of the cohort was 3 (0.6–7) y. Boys outnumbered girls by 1.5:1. The median (IQR) PRISM-12 score of the study population was 11 (6–16).

Table 1. Comparison of Baseline Parameters of Low and High Driving Pressure Groups

Baseline Characteristics	Total ($N = 101$)	Low ΔP ($n = 47$)	High ΔP ($n = 54$)	P
Age, y	2.9 (0.8–7.7)	2.8 (0.8–5.8)	2.9 (0.8–7.6)	.39
Comorbid illness present	29 (29)	14 (30)	15 (28)	.8
PRISM-12 score	11 (6–17)	8 (5–15)	13 (8–18)	.004
P_{aO_2}/F_{IO_2}	179 (100–212)	197 (160–212)	164 (100–208)	.03
Oxygenation index	6.3 (4.5–12)	5.3 (4.5–6.3)	7.1 (5.4–12.6)	.01
PEEP, cm H_2O	7 (6–9)	6 (5–7)	8 (6–10)	<.001
Organ dysfunction				
Renal	25 (25)	10 (21)	15 (28)	.45
Cardiac	38 (38)	15 (32)	23 (43)	.25
Hepatic	23 (23)	8 (17)	15 (28)	.19
Central nervous system	16 (16)	6 (13)	10 (18)	.26
Hematologic	44 (44)	17 (37)	27 (50)	.16
MODS	57 (57)	21 (45)	36 (67)	.03
Ionotropic score		0 (0–18)	1 (0–30)	.13

Data are presented as median (interquartile range) or n (%).
ΔP = dynamic driving pressure
Low ΔP = < 15 cm H_2O
High ΔP = ≥ 15 cm H_2O
PRISM-12 = Pediatric Risk of Mortality within first 12 h
MODS = multi-organ dysfunction syndrome

Common diagnoses were pneumonia ($n = 51$), severe sepsis with ARDS ($n = 24$), severe dengue infection ($n = 10$), aspiration pneumonia ($n = 7$), and drowning ($n = 4$). ARDS criteria as per PALICC 2015 were fulfilled by 65 subjects.[16] Nearly half of these subjects ($n = 32$, 49%) had mild ARDS (oxygenation index 4–8), a quarter ($n = 16$, 24.6%) had moderate ARDS (oxygenation index 8–16), and the rest had severe ARDS (oxygenation index ≥ 16).

The median (IQR) maximum PEEP provided in the first 24 h was 7 (6–9) cm H_2O. The majority of the children ($n = 66$, 65.3%) were ventilated with lung-protective ventilation (≤ 6 mL/kg ideal body weight), while the rest ($n = 35$, 34.7%) received tidal volume > 6 mL/kg ideal body weight. The group with low ΔP (< 15 cm H_2O) constituted nearly half of the subjects ($n = 47$, 46.5%), with the group with high ΔP (≥ 15 cm H_2O) having 54 subjects (53.5%). Baseline parameters in both groups are provided in Table 1.

In comparison to the high ΔP group, subjects in the low ΔP group had significantly shorter duration of ventilation, ICU length of stay, and hospital length of stay, and more ventilator-free days at day 28 (Table 2). However, there was no statistically significant difference in mortality between the 2 groups (17% in the low ΔP group vs 24% in the high ΔP group, $P = .38$). The minimum ΔP value above which a significant increase in mortality was present was 19 cm H_2O, as given by receiver operating characteristic curves (Fig. 1). Subgroup analysis of 65 subjects with ARDS yielded similar results with respect to mortality and other outcome parameters (Table 2). Logistic regression analysis showed that ΔP with a cutoff of 15 cm H_2O was an independent predictor of morbidity (odds ratio 3.2 [95% CI 1.2–9.0]) (Table 3).

Table 2. Comparison of Outcome Parameters in Both Driving Pressure Groups

Outcome	Low ΔP ($n = 47$)	High ΔP ($n = 54$)	P
ARDS, n	29	36	
Duration of ventilation, d			
Total	5 (4–6)	8 (6–11)	< .001
ARDS	6 (4–7)	9 (6–12)	< .001
Ventilator-free days at day 28, d			
Total	23 (20–24)	17 (0–22)	< .001
ARDS	22 (19–23)	16 (0–21)	< .001
ICU length of stay, d			
Total	6 (5–8)	12 (7–15)	< .001
ARDS	7 (6–9)	14 (7–15)	< .001
Hospital length of stay, d			
Total	11 (7–14)	18 (13–25)	< .001
ARDS	12 (8–15)	19 (13–25)	< .001
In-hospital mortality, %			
Total	17	24	.38
ARDS	18	25	.33

Data are presented as median (interquartile range) unless otherwise noted.
Total = total cohort of subjects with acute hypoxemic respiratory failure
ΔP = dynamic driving pressure
Low ΔP = < 15 cm H_2O
High ΔP = ≥ 15 cm H_2O

In-hospital mortality occurred in 21 (20.7%) children. Oxygenation index ≥ 8 and cumulative fluid balance

≥ 5% were significant independent predictors of mortality after multivariate analysis (Table 4). ΔP, even with a value of 19 cm H_2O (ie, the minimum value found to have association with mortality in the univariate analysis), was not an independent predictor of mortality. In children with ARDS, adjunct treatment measures were used in some subjects: steroids (n = 16, 24%), neuromuscular blockers (n = 24, 36.9%), rescue high-frequency oscillation ventilation (n = 9, 14%), prone position ventilation (n = 3), and extracorporeal membrane oxygenation (n = 3).

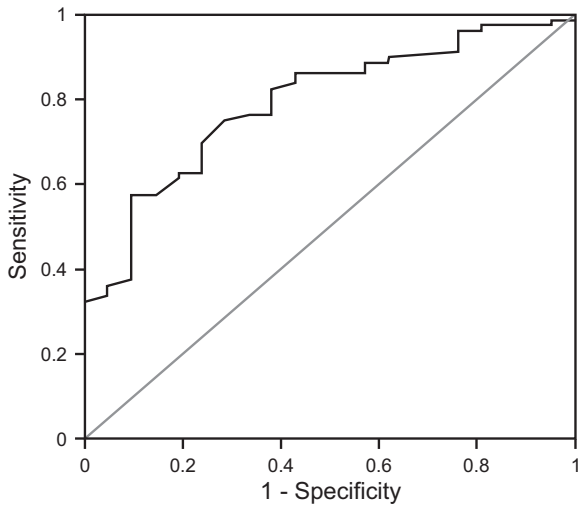

Fig. 1. Receiver operating characteristic curve for dynamic airway driving pressure as a predictor of mortality > 19 cm H_2O. The area under the curve = 0.81.

Discussion

Below a dynamic driving pressure safety threshold of 15 cm H_2O, the cutoff suggested by Bugedo et al,[7] our study showed lower morbidity as evidenced by a shorter duration of ventilation and shorter ICU and hospital length of stay without a significant difference in mortality. Baseline oxygenation parameters of the two ΔP groups were different. Hence the logistic regression models were made, which demonstrated the association of lower driving pressure with lower morbidity, after adjusting for differences in variables like P_{aO_2}/F_{IO_2}. The minimum ΔP cutoff that had an association with mortality was 19 cm H_2O in univariate analysis, but this was not significant when accounting for the confounding variables. Few studies in adult populations, including the large observational study to understand the global impact of severe acute respiratory failure (LUNGSAFE), demonstrate an association between driving pressure and mortality.[6,22] After the only known pediatric study also showed no association with mortality, it was argued that driving pressure might not be a useful parameter in pediatric ARDS.[23,24] Our study indicates that there is an association between driving pressure and morbidity, though it doesn't establish causality. Because there were only 21 deaths, we were probably underpowered to detect an association with mortality (post-hoc power = 52%). It is

Table 3. Logistic Regression Model to Find Predictors of Morbidity

Variables	With Significant Morbidity (n = 41)	Without Significant Morbidity (n = 60)	P*	Adjusted Odds Ratio (95% CI)	P†
Age, months	23 (7–70)	35 (7–85)	.38		
Diagnosis			.39		
Pneumonia	21 (51.2)	30 (50)			.54
Sepsis	12 (29.2)	12 (20)			.34
Severe dengue	4 (9.7)	6 (10)			.66
Aspiration	3 (7.3)	4 (6.6)			.36
PRISM-12 score			< .001	2.9 (1.1–7.9)	.03
≤ 12	14 (34.2)	43 (71.6)			
> 12	27 (65.8)	17 (28.4)			
Oxygenation index			.002		.11
< 8	21 (51.2)	48 (80)			
≥ 8	19 (48.8)	11 (20)			
MODS	30 (73)	27 (45)	< .001	3.4 (1.1–10.4)	.03
Driving pressure, cm H_2O			< .001	3.2 (1.2–9.0)	.02
< 15	10 (24.4)	37 (61.6)			
≥ 15	31 (75.6)	23 (38.3)			

Data are presented as median (interquartile range) or n (%). Significant morbidity = ventilation > 7 d and ICU length of stay > 10 d, or death.
* Univariate analysis.
† Multivariate analysis.
PRISM-12 = Pediatric Risk of Mortality within first 12 h
MODS = multi-organ dysfunction syndrome

Table 4. Logistic Regression Model to Find Early Mortality Predictors

Variable	In-Hospital Mortality ($n = 21$)	Survived to Discharge ($n = 80$)	P*	Adjusted Odds Ratio (95% CI)	P†
Diagnosis					
Pneumonia	10 (47.6)	41 (51.2)	.30		.99
Sepsis	8 (38)	16 (20)			.99
Severe dengue	2 (9.5)	8 (10)			.99
Aspiration	1 (4.7)	6 (7.5)			.99
Driving pressure, cm H_2O				Not reported	
< 19	13 (62)	66 (82.5)	.04		.46
≥ 19	8 (38)	14 (17.5)			
Oxygenation index				6.1 (1.7 – 22.5)	.007
< 8	8 (38)	61 (76)	.001		
≥ 8	13 (62)	19 (24)			
MODS	18 (85.7)	39 (48.7)	.003		.09
Fluid balance, %‡				4.5 (1.1 – 18.7)	.04
≤ 5	10 (47.6)	70 (87.5)	$< .001$		
> 5	11 (52.4)	10 (12.5)			

Data are presented as *n* (%).
* Univariate analysis.
† Multivariate analysis.
‡ Cumulative fluid balance at 48 h.
MODS = multi-organ dysfunction syndrome

also possible that lung stress and the resultant ventilator-induced lung injury in children, which driving pressure tries to primarily represent, has more effect on morbidity parameters like duration of ventilation than mortality. There is a lack of literature about ventilator-induced lung injury and its effects in children that should be addressed in future studies.

An interesting finding from this study was that more than half of the subjects (38 of 66, 57.5%) in the lung-protective ventilation cohort ($<$ 6 mL/kg low tidal volume) still had high driving pressure (ie, $\geq$ 15 cm H_2O). This indicates that the lung-protective tidal volumes with which these children were ventilated were not really low because they had high driving pressures indicating increased lung stress and strain that is thought to contribute to morbidity. While the concept of a safe limit for driving pressure is intriguing, it is an important to point out that neither the validity of a safe limit nor the management of mechanical ventilation by controlling the driving pressure has been subjected to high-quality trials. The relatively new concept of driving pressure was not addressed by PALICC 2015[16] as a parameter to be monitored in pediatric ARDS due to the lack of pediatric data.[25] The PALICC recommendations had suggested limiting tidal volume to 5–8 mL/kg (3–6 mL/kg for severe disease), aiming to limit PIP. We feel that monitoring driving pressure may guide clinicians to individualize the tidal volumes and to decide when to use or accept lower tidal volumes than the conventional 6 mL/kg in ARDS.

Another important finding is that an oxygenation index $>$ 8 was an independent early predictor of mortality, while driving pressure was not (even with a cutoff of 19 cm H_2O). Similar findings of variables of oxygenation being better predictors of mortality than parameters of lung mechanics in pediatric ARDS were reported by Yehya and Thomas.[23] Our findings also support the notion that parameters of oxygenation may reflect the overall functional severity of lung disease better and thys may have better prognostic value in pediatric ARDS.

Our study is the first to evaluate the impact of airway driving pressure on mortality and morbidity parameters separately in children. Reasonable sample size and inclusion of a broad group of subjects with acute hypoxemic respiratory failure were important strengths. It should be noted that we defined ΔP as the difference between PIP and PEEP, as all children were ventilated with decelerating flow. We agree that this was a limitation of the study because PIP partly accounts for the resistance component also. Hence, the calculated dynamic airway driving pressure likely overestimated the actual driving pressure in at least some of the subjects. However, studies have shown that the PIP-to-plateau pressure gradient is minimal with decelerating flow.[26,27] Moreover, modes like pressure control and pressure-regulated volume control, which use decelerating flow patterns, are more commonly used in pediatric ARDS.[28,29] Hence, our findings might hold relevance in children with ARDS and may have implications for further research. Multicenter prospective studies in children are needed to guide us further and to clearly establish the use of driving pressure for optimization of mechanical ventilation in pediatric ARDS.

Conclusions

Our study showed an association between dynamic driving pressure and outcomes in pediatric ARDS with the threshold of 15 cm H_2O being significant in increasing morbidity. Whether a threshold value should be associated with mortality needs to be tested in a larger sample, preferably in a multi-center study. Further research is required in pediatric ARDS regarding the association of lung stress and strain affecting both short-term and long-term outcomes.

REFERENCES

1. Slutsky AS. Basic science in ventilator-induced lung injury: implications for the bedside. Am J Respir Crit Care Med 2001;163(3 Pt 1):599-600.
2. Carrasco Loza R, Villamizar RG, Medel FN. Ventilator-induced lung injury (VILI) in acute respiratory distress syndrome (ARDS): volutrauma and molecular effects. Open Respir Med J 2015;9:112-119.
3. Luigi C, Nicholas H. Lung protective ventilation (editorial). BMJ 2012;344:e2491.
4. Gattinoni L, Pesenti A. The concept of baby lung. Intensive Care Med 2005;31(6):776-784.
5. Chiumello D, Carlesso E, Brioni M, Cressoni M. Airway driving pressure and lung stress in ARDS patients. Crit Care 2016;20:276-280.
6. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015;372(8):747-755.
7. Bugedo G, Retamal J, Bruhn A. Driving pressure: a marker of severity, a safety limit, or a goal for mechanical ventilation? Crit Care 2017;21 (1):199.
8. Guerin C, Papazian L, Reignier J, Ayzac L, Loundou A, Forel JM, Investigators of theAcurasys and Proseva Trials. Effect of driving pressure on mortality in ARDS patients during lung protective mechanical ventilation in two randomized controlled trials. Crit Care 2016;20(1):384.
9. Chiu LC, Hu HC, Hung CY, Chang CH, Tsai FC, Yang CT, et al. Dynamic driving pressure associated mortality in acute respiratory distress syndrome with extracorporeal membrane oxygenation. Ann Intensive Care 2017;7(1):12.
10. Villar J, Martín-Rodríguez C, Domínguez-Berrot AM, Fernández L, Ferrando C, Soler JA, et al. A quantile analysis of plateau and driving pressures: effects on mortality in patients with acute respiratory distress syndrome receiving lung-protective ventilation. Crit Care Med 2017;45(5):843-850.
11. Khemani RG, Conti D, Alonzo TA, Bart RD 3rd, Newth CJ. Effect of tidal volume in children with acute hypoxemic respiratory failure. Intensive Care Med 2009;35(8):1428-1437.
12. Foglia E, Meier MD, Elward A. Ventilator-associated pneumonia in neonatal and pediatric intensive care unit patients. Clin Microbiol Rev 2007;20(3):409-425.
13. Phillips S, Edlbeck A, Kirby M, Goday P. Ideal body weight in children. Nutr Clin Pract 2007;22(2):240-245.
14. Falde S, Holets S, Marini JJ, Oeckler RA, Cortes Puentes GA. Dynamic airway driving pressure and mechanical power across the lung and respiratory system in acute respiratory distress syndrome (ARDS) (abstract). Am J Respir Crit Care Med 2020;201:A4100.
15. GoldsteinB GB, Randolph A. International pediatric sepsis consensus conference. Definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med 2005;6(1):2-8.
16. Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med 2015;16(5):428-439.
17. Gupta S, Sankar J, Lodha R, Kabra SK. Comparison of prevalence and outcomes of pediatric acute respiratory distress syndrome using pediatric acute lung injury consensus conference criteria and Berlin definition. Front Pediatr 2018;6:93.
18. Wong JJ, Loh TF, Testoni D, Wong JJ, Loh TF, Testoni D. Epidemiology of pediatric acute respiratory distress syndrome in Singapore: risk factors and predictive respiratory indices for mortality. Front Pediatr 2014;2:78.
19. Panico FF, Troster EJ, Oliveira CS, Faria A, Lucena M, João PRD, et al. Risk factors for mortality and outcomes in pediatric acute lung injury/acute respiratory distress syndrome. Pediatr Crit Care Med 2015;16(7):e194-e200.
20. Flori HR, Glidden DV, Rutherford GW, Matthay MA. Pediatric acute lung injury: prospective evaluation of risk factors associated with mortality. Am J Respir Crit Care Med 2005;171(9):995-1001.
21. Rosenberg AL, Dechert RE, Park PK, Bartlett RH, NIH NHLBI ARDS Network. Review of a large clinical series: association of cumulative fluid balance on outcome in acute lung injury: a retrospective review of the ARDSnet tidal volume study cohort. J Intensive Care Med 2009;24(1):35-46.
22. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA 2016;315(8):788-800.
23. Yehya N, Thomas NJ. Disassociating lung mechanics and oxygenation in pediatric acute respiratory distress syndrome. Crit Care Med 2017;45(7):1232-1239.
24. Inata Y, Takeuchi M. Does driving pressure matter in pediatric acute respiratory distress syndrome? Strain to find the answer. Crit Care Med 2017;45(11):e1196-e1197.
25. Emeriaud G, Newth CJ, Pediatric Acute Lung Injury Consensus Conference Group. Monitoring of children with pediatric acute respiratory distress syndrome: Proceedings from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med 2015;16(5 Suppl 1):S86-S101.
26. Maung AA, Johnson DC, Luckianow GM, Kaplan LJ. Ventilator gas delivery waveform substantially impacts plateau pressure and peak-to-plateau pressure gradient determination. J Trauma Acute Care Surg 2015;78(5):976-979.
27. Guldager H, Nielsen S, Carl P, Soerensen M. A comparison of volume control and pressure-regulated volume control ventilation in acute respiratory failure. Crit Care 1997;1(2):75-77.
28. Khemani RG, Newth CJ. The design of future pediatric mechanical ventilation trials for acute lung injury. Am J Respir Crit Care Med 2010;182(12):1465-1474.
29. Santschi M, Jouvet P, Leclerc F, Gauvin F, Newth CJ, Carroll CL, et al. Acute lung injury in children: therapeutic practice and feasibility of international clinical trials. Pediatr Crit Care Med 2010;11(6):681-689.