Have changes in ventilation practice improved outcome in children with acute lung injury?*

Waleed H. Albuali, MD; Ram N. Singh, MD, FRCPC; Douglas D. Fraser, MD, PhD, FRCPC; Jamie A. Seabrook, MA; Brian P. Kavanagh, MD, FRCPC; Christopher S. Parshuram, MD, FRACP; Alik Kornecki, MD

Objectives: **To describe the changes that have occurred in mechanical ventilation in children with acute lung injury in our institution over the last 10–15 yrs and to examine the impact of these changes, in particular of the delivered tidal volume on mortality.**

Design: **Retrospective study.**

Setting: **University-affiliated children's hospital.**

Patients: **The management of mechanical ventilation between 1988 and 1992 (past group, n = 79) was compared with the management between 2000 and 2004 (recent group, n = 85).**

Interventions: **None.**

Measurements and Main Results: **The past group patients were ventilated with a significantly higher mean tidal volume (10.2 ± 1.7 vs. 8.1 ± 1.4 mL·kg^{-1} actual body weight, $p < .001$), lower levels of positive end-expiratory pressure (6.1 ± 2.7 vs. 7.1 ± 2.4 cm H_2O, $p = .007$), and higher mean peak inspiratory pressure (31.5 ± 7.3 vs. 27.8 ± 4.2 cm H_2O, $p < .001$) than the recent group patients. The recent group had a lower mortality (21% vs. 35%, $p = .04$) and a greater number of ventilator-free days (16.0 ± 9.0 vs. 12.6 ± 9.9 days, $p = .03$) than the past group. A higher tidal volume was independently associated with increased mortality (odds ratio 1.59; 95% confidence interval 1.20, 2.10, $p < .001$) and reduction in ventilation-free days (95% confidence interval −1.24, −0.77, $p < .001$).**

Conclusions: **The changes in the clinical practice of mechanical ventilation in children in our institution reflect those reported for adults. In our experience, mortality among children with acute lung injury was reduced by 40%, and tidal volume was independently associated with reduced mortality and an increase in ventilation-free days. (Pediatr Crit Care Med 2007; 8:324–330)**

Key Words: children; tidal volume; mechanical ventilation; acute lung injury; acute respiratory distress syndrome; mortality

The reduction in tidal volume (Vt) administered during mechanical ventilation (MV) is the only intervention that has been shown to affect survival in adults with acute lung injury (ALI) (1). Although the optimal Vt (2–4), airway pressure (5), and alternative approaches to ventilatory management in the setting of ALI (6) are still controversial issues, it is clear that the use of Vt >12 mL·kg^{-1} predicted body weight (PBW) increases mortality in adults suffering from ALI, compared with Vt of 6 mL·kg^{-1} PBW (7).

The optimal management for adults with ALI or acute respiratory distress syndrome (ARDS) remains unresolved, and the situation is even less clear for children. Virtually all the laboratory investigations of ventilator-induced lung injury have focused on adult animal models (8), and most of clinical studies were carried out in adult patients (7, 9–12).

Notwithstanding its lower incidence in the pediatric population, ALI bears an associated mortality of 22% to 27% in affected children (13, 14). Lacking primary data in children, various authors have suggested a number of approaches, all of which have been extrapolated from the literature on adults. However, three lines of evidence raise concerns with such an approach. First, contrary to empirical impressions of their greater vulnerability, recent laboratory data suggest that the neonatal (15) and infant (16) lungs are less—not more—vulnerable to the effects of high Vt. Second, the single recent clinical study that did examine the influence of Vt on outcome in pediatric ARDS (a retrospective case series) (13) indicated that Vt may not be an independent predictor of outcome. Third, it is known that very low Vts increase the propensity for development of atelectasis (17) or, as has been suggested by some, that low Vts may increase mortality (2, 3). If this were true, the effects might be greater in infants and children because their lower functional residual capacity (18), and their more compliant chest wall (19) could further increase the predilection to atelectasis and the potentially associated poor outcome. Thus, it is important to verify the appropriateness of applying adult recommendations for MV in the pediatric setting.

The effect of Vt on mortality should ideally be investigated in a prospective randomized clinical trial. We conducted a retrospective study due to ethical constraints associated with exposing children to a strategy of MV that has been found to be harmful in adults (7). We chose to first compare the clinical practice of MV between 1988 and 1992, when protective strategies of ventilation were less likely to have been applied, to a more recent period (2000–2004) during which protective strategies of MV were established in

*See also p. 397.

From the Department of Pediatrics and Pediatric Critical Care Unit, Children's Hospital of Western Ontario, London Health Sciences Center, University of Western Ontario, London, ON, Canada (WHA, RNS, DDF, JAS, AK); and the Departments of Pediatrics and Critical Care, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada (BPK, CSP).

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For information regarding this article, E-mail: alik.kornecki@lhsc.on.ca

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adults. Second, we investigated the impact of various variables, principally ventilation variables, on mortality and length of ventilation.

MATERIALS AND METHODS

The study protocol was reviewed and approved by the Institutional Research Ethics Board of the University of Western Ontario. All ventilated pediatric patients with ALI during 1988–1992 (past group) were compared with patients admitted during 2000–2004 (recent group). The primary outcome measured was mortality in the pediatric critical care unit (PCCU), and the secondary outcome was ventilator-free days. All children between the ages of 1 wk and 17 yrs who were hospitalized at the PCCU (12 beds, medical/surgical tertiary care unit) in the university-affiliated Children's Hospital of Western Ontario and who had been mechanically ventilated were identified and screened for fulfilling the inclusion criteria. All patients who required MV were identified in the PCCU database and in the hospital's computerized (after 1991) and noncomputerized (before 1991) medical records according to the *International Classification of Diseases, Ninth Revision*. The medical records of identified patients were further reviewed, and all patients were screened for ALI. ALI was defined as acute onset of hypoxemia (Pao_2/Fio_2 <300) with no clinical evidence of left atrial hypertension and with bilateral lung infiltrates on chest radiograph as interpreted by the staff radiologist or PCCU staff physician (20). ARDS was defined as ALI with Pao_2/Fio_2 <200. We excluded patients with underlying chronic lung disease, unresolved congenital heart disease, severe head trauma (Glasgow Coma Scale score <8), diaphragmatic hernia, or congenital metabolic or neuromuscular diseases as well as patients who required extracorporeal membrane oxygenation and those who developed brain death or had life-support restriction on admission. Chronic lung disease was defined as the need for oxygen at home. Two patients who received liquid ventilation were also excluded.

The data collected for each patient included demographics, diagnosis, results of blood gas measurements, adjuvant therapies, ventilation variables, duration of ventilation, ventilator-free days, and in-PCCU mortality. Ventilator-free days were defined as the number of days the patient did not require MV during the 28 days from initiation of MV. A value of zero was assigned to patients who died (7). Patients who required reintubation within 72 hrs from extubation were considered as failed extubation, and these days were calculated as ventilation days. Patients who required reintubation >72 hrs of extubation were considered as a new patient in case they met the inclusion criteria. Each day for the first 3 days of ventilation, ventilation data were collected from the ventilator flow sheet at approximately noontime (10 am to 2 pm), or we used the first data available after 6 am when the former were missing. V_T was defined as the exhaled V_T of assisted breath with no pressure support as measured by the ventilator. When the patient was on high-frequency oscillation ventilation, V_T was not collected. Corresponding measurements of arterial blood gases were collected. Adjuvant therapies were defined as the introduction of nitric oxide (>6 hrs), prone positioning (>12 hrs/day or >6 hrs/day for two consecutive days), surfactant administration, and the application of high-frequency oscillation ventilation (>12 hrs, within ≥1 day). Pediatric Risk of Mortality (PRISM) III (21) on the first day (after 12 hrs) was calculated for each patient. Oxygenation index (OI = Fio_2·mean arterial pressure/Pao_2), Pao_2/Fio_2, and ventilation index (respiratory rate·[peak inspiratory pressure {PIP} − positive end-expiratory pressure {PEEP}]·$Paco_2$)/1000) were calculated for each patient for the first 3 days of MV.

Statistical Analysis. Continuous variables were reported as mean ± SD unless otherwise stated. The chi-square test was used to compare proportions, and independent samples Student's *t*-tests (or Mann-Whitney test where applicable) were used to compare continuous variables between groups. We considered $p <$ .05 as statistically significant, except when the Bonferroni adjustment was made for multiple comparisons. Logistic regression was used to determine which variables were associated with mortality. Multiple regression was performed to assess the relationship between predictive risk factors and duration of mechanical ventilation.

RESULTS

Baseline Characteristics. A total of 164 children were included in the study. The past group (1988–1992) consisted of 79 children from a total of 3,360 (2.35%) admissions and 1,647 (4.8%) ventilated children, and the recent group (2000–2004) consisted of 85 children from a total of 3,523 (2.41%) admissions and 1,815 (4.7%) ventilated children. Demographic data and initial patients' characteristics are shown in Tables 1 and 2.

Mechanical Ventilation and Adjuvant Therapies. During the first 3 days of ventilation, the mean V_T, PIP, and Pao_2 values were significantly lower, and the mean PEEP and $Paco_2$ values were significantly higher in the recent group compared with the past group (Table 3). Fifty-three percent of patients in the recent group received a mean V_T <8 mL·kg^{-1}, and 23.5% received <7 mL·kg^{-1} actual body weight (ABW) compared with 5.6% and 1.4%, respectively, in the past group. No significant difference between groups in the proportion of volume or pressure control ventilation used was observed (Table 3).

Inhaled nitric oxide was administered in 1.3% (1 of 79) of patients in the past group compared with 31% (26 of 85) in the recent group ($p < .001$). High-frequency oscillation ventilation was used in 4% (3 of 79) of patients in the past group compared with 24% (20 of 85) in the recent group ($p = .003$). Prone positioning was used in 1.3% (1 of 79) of patients in the past group compared with 21% (18 of 85) in the recent group ($p <$ .001), and surfactant was administered to 8% (6 of 79) of patients in the past group compared with 33% (28 of 85) in the recent group ($p = .002$). Seventeen percent of patients in the recent group compared with none in the past group received a combination of two or more adjuvant therapies ($p < .001$) (data not shown).

Disease and Ventilation Outcomes. The mortality rate in the recent group was significantly lower than in the past group (21 vs. 35%, respectively, $p =$ .04) (Table 2) even though the mean OI

Table 1. Baseline characteristics of patients in both study groups

	Past (1988–1992) (n = 79)	Recent (2000–2004) (n = 85)	*p* Value
Age, yrs[a]	1.3 (3.4)	2.6 (7.7)	.56
Weight, kg[a]	10.1 (15)	12.0 (18.8)	.68
Male, %	50.6	65.9	.048
PRISM III	11.3 ± 4.9	11.1 ± 5.6	.87
Peak compliance, mL·kg^{-1}·cm H_2O^{-1}[b]	0.40 ± 0.09	0.41 ± 0.12	.68

PRISM, Pediatric Risk of Mortality.

[a]Median and interquartile range (Mann-Whitney test for differences); [b]peak compliance = (peak inspiratory pressure [cm H_2O]− positive end-expiratory pressure [cm H_2O])/tidal volume (mL·kg^{-1}).

Table 2. Mortality between study groups and according to underlying conditions[a]

	Past (1988–1992) (%)	Recent (2000–2004) (%)	*p* Value
Total	79	85	
Survivors	51 (65)	67 (79)	.04
Nonsurvivors	28 (35)	18 (21)	
Immunodeficiency			
Total	13 (16)	13 (15)	.84
Survivors	5 (38)	5 (38)	.99
ARDS[b]			
Total	58 (73)	72 (85)	.08
Survivors	33 (57)	54 (75)	.03
Sepsis			
Total	26 (33)	29 (34)	.87
Survivors	9 (35)	19 (66)	.02
Pneumonia (bacterial and viral)			
Total, %	26 (33)	31 (42)	.63
Survivors	21 (81)	25 (81)	.99
Aspiration pneumonia			
Total, %	3 (4)	6 (5)	.93
Survivors	2 (75)	6 (100)	.13
Respiratory syncytial virus			
Total, (%)	13 (16)	12 (14)	.68
Survivors	13 (100)	12 (100)	.99
Trauma (lung contusion)			
Total, %	4 (5)	2 (2)	.36
Survivors	3 (75)	2 (100)	.44
Near drowning and drowning			
Total	4 (5)	3 (3)	.63
Survivors	3 (75)	2 (100)	.81
Others			
Total	3 (5)	3 (2)	.93
Survivors	0 (0)	1 (33)	.27

ARDS, acute respiratory distress syndrome.
[a]Because of rounding, not all percentages total 100; [b]Pao_2/Fio_2 <200.

Table 3. Modality of ventilation and mean respiratory and ventilatory values during the first 3 days of ventilation

	Past (1988–1992) (n = 79)	Recent (2000–2004) (n = 85)	p^a Value
Vt, mL·kg^{-1}	10.2 ± 1.7 (211)	8.1 ± 1.4 (233)	<.001
PIP, cm H_2O	31.5 ± 7.3 (223)	27.8 ± 4.2 (233)	<.001
PEEP, cm H_2O	6.1 ± 2.7 (223)	7.1 ± 2.4 (232)	.007
$Paco_2$, mm Hg	37.0 ± 5.0 (225)	47.2 ± 11.8 (231)	<.001
Pao_2, mm Hg	84.4 ± 14.4 (225)	78.9 ± 14.9 (245)	.017
OI	14.7 ± 5.0 (223)	17.7 ± 5.3 (232)	<.001
Pao_2/Fio_2	153.0 ± 59.9 (225)	139.2 ± 53.1 (239)	.12
VI	28.4 ± 13.6 (225)	28.6 ± 15.6 (235)	.94
PC, %	52 (225)	55 (245)	.99
VC, %	47 (225)	37 (245)	.02
HFOV, %	1 (225)	8 (245)	<.001

Vt, tidal volume; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; OI, oxygenation index; VI, ventilation index; PC, pressure control; VC, volume control; HFOV, high-frequency oscillatory ventilation.
[a]Independent samples *t*-tests with the Bonferroni correction ($p = .05/3 = .017$) were used to test for significant differences between the groups. In parentheses, the number of ventilation days.

was significantly higher and the Pao_2/Fio_2 was significantly lower at baseline in the recent group (Table 3). The significant improvement in survival is also illustrated by the survival curves (Fig. 1). There were more ventilation-free days in the recent group compared with the past group (16.0 ± 9.1 vs. 12.7 ± 10 days, $p = .03$). The duration of ventilation in children who survived to discharge from the PCCU in the recent group was not significantly different compared with the past group (8.3 ± 4.0 vs. 7.6 ± 3.9, $p = .36$).

Variables Associated With Increased Mortality and Length of Ventilation. The variables significantly associated with mortality and/or ventilation-free days by univariate analysis (Table 4) were subsequently entered into multivariable regression analyses (Table 5). The multivariable logistic regression analysis revealed that PRISM III, immunodeficiency, and Vt were independently associated with increased mortality (Table 5). Multiple regression revealed that these same factors as well as male gender were associated with a reduction in ventilation-free days. No correlations between Vt and severity of lung disease (ventilation index, OI, and Pao_2/Fio_2) and PRISM III were found (data not shown). A weak but significant relationship was observed between PIP and Vt on the first day ($r = 0.23$, $p = .01$) of ventilation, and it increased when evaluated for means in 3 days of ventilation ($r = 0.37$ $p < .001$) (22). No significant interaction effects were observed between PIP, $Paco_2$, respiratory compliance, PEEP, and Vt on mortality (data not shown).

DISCUSSION

The main findings of this study are as follows: 1) The clinical approach to MV in children with ALI has changed over the last 15 yrs and follows most of the adult MV recommendations; and 2) the mortality in this population decreased by 40% over the same period, and higher Vt was independently associated with increased mortality and decreased ventilation-free days.

The mortality rate observed in the recent group (21%) is similar to the figures recently published in the pediatric literature (13, 14, 23, 24) and is lower than that recently reported among adults (7, 25). The mortality rate for the past group (35%) is lower than what had been reported by others within the same time frame in children with acute respiratory failure or ARDS (62% to 82%) (26, 27), which may be explained by the different definition of ARDS used in previous studies (e.g., Lung Injury Score >2.5) (27).

There were more ventilation-free days in the recent group than in the past group (16.0 ± 9.1 vs. 12.7 ± 10 days, $p = .03$), but the duration of ventilation for children who survived to discharge from the unit was not different between the two groups (8.3 ± 4.0 vs. 7.6 ± 3.9 days, $p = .36$). This latter finding suggests that the differences in ventilation-free days may be attributed to the reduction in mortality in the recent group rather than to the reduction of ventilation duration among the survivors (28).

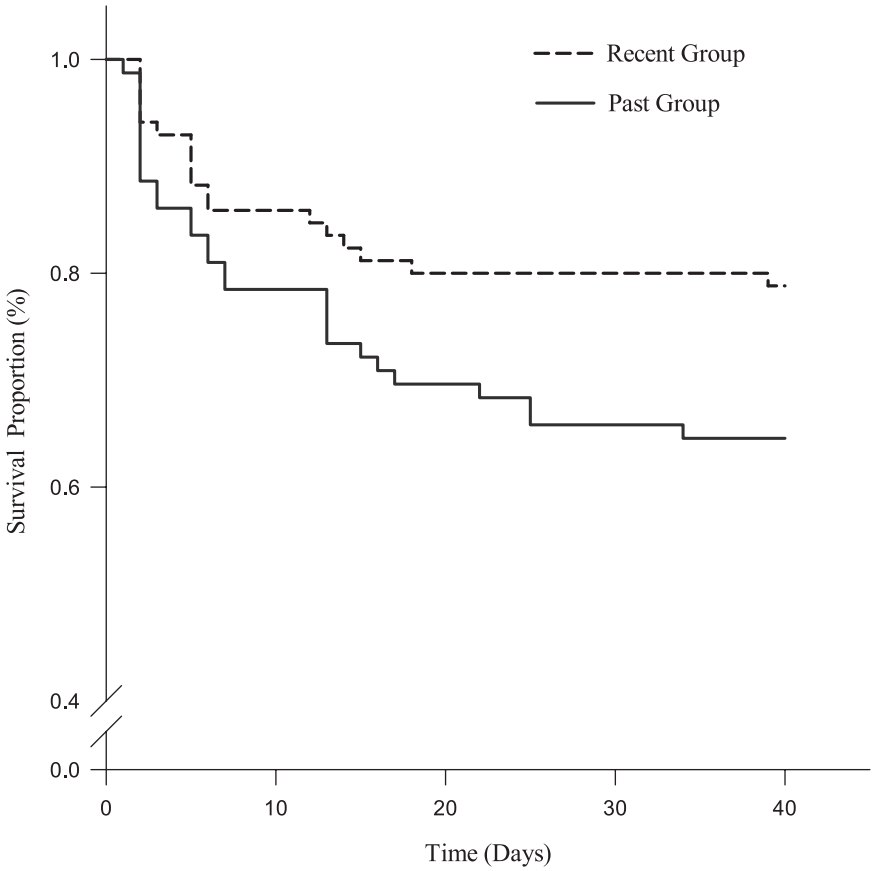

Figure 1. Kaplan-Meier estimates of survival among recent and past acute lung injury patients, showing significantly better survival in the recent group ($p < .041$; log rank test). All patients who survived 40 days survived discharge from the critical care unit.

Table 4. Univariate analysis for clinical variables associated with mortality

Variable	Odds Ratio	95% CI	*p* Value
Age in days	1.00	0.99, 1.00	.50
Age ≤1 yr	0.57	0.28, 1.18	.13
Group (recent vs. past group)	0.49	0.25, 0.98	.04
Male gender	0.43	0.21, 0.85	.02
Immunodeficiency	5.76	2.37, 13.99	<.001
Pneumonia	0.44	0.19, 1.00	.046
Sepsis	4.21	2.04, 8.70	<.001
Surfactant	1.54	0.69, 3.44	.29
HFOV	2.22	0.90, 5.51	.08
Nitric oxide	1.34	0.55, 3.24	.52
Prone position	2.60	1.01, 6.90	.048
PP + NO + surfactant	3.48	0.89, 13.57	.07
Pneumothorax	1.55	0.60, 3.99	.36
$Paco_2$[a]	0.98	0.95, 1.01	.13
Pao_2[a]	1.00	0.98, 1.01	.64
PIP[a]	1.08	1.02, 1.15	.01
PEEP[a]	1.13	1.00, 1.28	.06
VT[a]	1.34	1.09, 1.65	.006
Pao_2/Fio_2	0.99	0.97, 1.02	.14
Pao_2/Fio_2 <200	5.11	1.48, 17.65	.005
Ventilation index	1.00	0.98, 1.03	.71
Oxygenation index	1.00	0.93, 1.06	.87
PRISM III	1.35	1.22, 1.49	<.001
Compliance	0.19	0.01, 6.61	.36

HFOV, high-frequency oscillatory ventilation; PP, prone positioning; NO, nitric oxide; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; VT, tidal volume; PRISM, Pediatric Risk of Mortality.

[a]Mean for the first 3 days of ventilation.

Multivariable logistic regression analysis revealed that only VT, PRISM III, and immunodeficiency were associated with increased mortality, while immunodeficiency, male sex, PRISM III, prone positioning, and VT were associated with ventilation-free days (Table 5). VT was the only therapeutic intervention found to be associated with mortality. VT was not associated with severity of lung disease (ventilation index, Pao_2/Fio_2, and OI), severity of illness (PRISM III), gender, age, or baseline respiratory system compliance when analyzed for both study groups or for the recent group separately (data not shown). The correlation between administered VT and mortality is shown in Figure 2. Despite similar baseline PRISM, Pao_2/Fio_2, and mean OI over the first 3 days, mortality tended to increase with increments of VT.

Randomized controlled trials for evaluating the effect of VT on mortality among adult patients with ALI and/or ARDS have revealed conflicting results (7, 9, 11, 12). However, reduction of the administered VT was the only therapeutic intervention to show improvement in mortality (7). Presumably, reduced mortality may be detected only when the low VT and limited plateau pressure (Pplat) are compared with the relatively high VT (12 $mL \cdot kg^{-1}$ PBW) and Pplat (29). The mean VT administered in the recent group for the first 3 days (8.1 ± 1.4 $mL \cdot kg^{-1}$ ABW) was higher than the VT administered in the ARDSNet study (6 $mL \cdot kg^{-1}$ PBW) (7). However, it better reflects the VT administered in clinical practice in adult critical care units (7, 30–33) and may better coincide with the recommendations suggesting that VT should be titrated according to severity of lung injury and lung compliance (2, 4–6, 8, 34).

Over the last 10–15 yrs, protective strategies of ventilation (35, 36) have been developed and implemented with full or partial success in adult critical care (30, 31, 37, 38). However, there are no data on the changes that took place in the practice of MV in children over the same time period. This study shows that pediatric patients in our center are now (recent group) being ventilated with significantly higher PEEP, lower PIP, and lower VT levels than 10–15 yrs ago (past group). Furthermore, higher $Paco_2$ and lower Pao_2 levels are currently tolerated compared with earlier findings (past group) (Table 3). These changes in MV practice reflect most of the adult critical care recommendations (6, 20, 39) and practice (31–33, 37) of the protective strategies of ventilation.

Since the Pplat pressures were not available, we collected the PIP level. The mean PIP level in the recent group (27.8 ± 4.2 cm H_2O) was similar to the Pplat in the ARDSNet trial (25–26 cm H_2O) (7). Since PIP is estimated to be 10% to 30% higher than Pplat, in essence the patients in this study most likely were ventilated with lower Pplat pressures than those applied in the ARDSNet trial as well as in other studies performed on adults (25, 31) and similar to the Pplat pressures used by others (25). The lower inflation pressure administered in pediatric patients may be attributed to the more compliant chest wall during development (19). A prospective study conducted in children by Flori et al. (13) reported a

Table 5. Multivariable analysis for clinical variables[a] associated with mortality and ventilation-free days

Variable	Odds Ratio	Mortality		Ventilation-Free Days	
		95% CI	*p* Value	95% CI	*p* Value
PRISM III	1.35	1.21, 1.50	<.001	−1.20, −0.66	<.001
Group (recent vs. past group)	0.86	−0.82, 0.99	.23	−6.21, 0.06	.06
Tidal volume[b]	1.59	1.20, 2.10	<.001	−1.99, −0.43	.003
PEEP[b]	1.08	0.83, 1.41	.56	−0.84, 0.46	.56
PIP[b]	0.95	0.88, 1.02	.15	−0.06, 0.50	.13
Pao_2/Fio_2 <200	3.58	0.45, 28.34	.23	−5.38, 1.44	.25
Immunodeficiency	3.58	1.09, 11.76	.04	−7.41, −0.32	.03
Male gender	0.44	0.17, 1.15	.09	0.44, 5.29	.02
Sepsis	1.75	0.49, 6.23	.39	−4.99, 1.25	.24
Pneumonia	1.64	0.50, 5.38	.42	−4.42, 1.60	.36
Prone position	3.14	0.67, 14.67	.15	−9.58, −0.17	.04
HFOV	0.65	0.13, 3.36	.61	−3.30, 5.49	.62

PRISM, Pediatric Risk of Mortality; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; HFOV, high-frequency oscillatory ventilation.

[a]Only for associated variables ($p \leq .1$) from univariate analysis; [b]mean for the first 3 days of ventilation.

higher VT (10 ± 4.9 mL·kg^{-1} PBW), higher PIP (30.6 ± 9.8 cm H_2O), and lower PEEP (5.3 ± 2.64 cm H_2O) than observed in the recent group but similar to the values observed in the past group. This may be attributed to the fact that the Flori et al. study was conducted from 1996 to 2000 (13), before the publication of the ARDSNet trial (7). Furthermore, Flori et al. did not detect an association between VT and mortality, most likely because there was no control arm. The finding that adjuvant therapies, other than surfactant administration, were almost exclusively administered to children in the recent group is not surprising, given that most of those therapies were introduced into clinical practice in the mid-1990s (40). Multivariable regression analyses failed to show an association between the application of these modalities and outcome. This is in accordance with previous studies with the exception of one randomized controlled trial that showed a reduction in mortality when surfactant was administered to children with ALI (41). Most studies that evaluated the efficacy of surfactant or other adjuvant therapies failed to show an improvement in outcome, and their benefits were limited to transient improvement in oxygenation (42, 43).

Our study has several limitations. Most of them arise from its retrospective nature. First, unmeasured variables, such as inotropic support, fluid management, antibiotics, sedation, early nutrition, and management practices by nursing and respiratory professionals, have changed over the last 8–15 yrs. Furthermore, since the ability to support organ failure (e.g., renal replacement therapy) has improved over the last decade and mortality in patients with ALI/ARDS has been shown to be associated with nonpulmonary multiorgan failure in children (13), it is impossible to exclude the potential contribution of these factors to the improvement in survival. By using a more recent period (e.g., 1996–2000 instead of

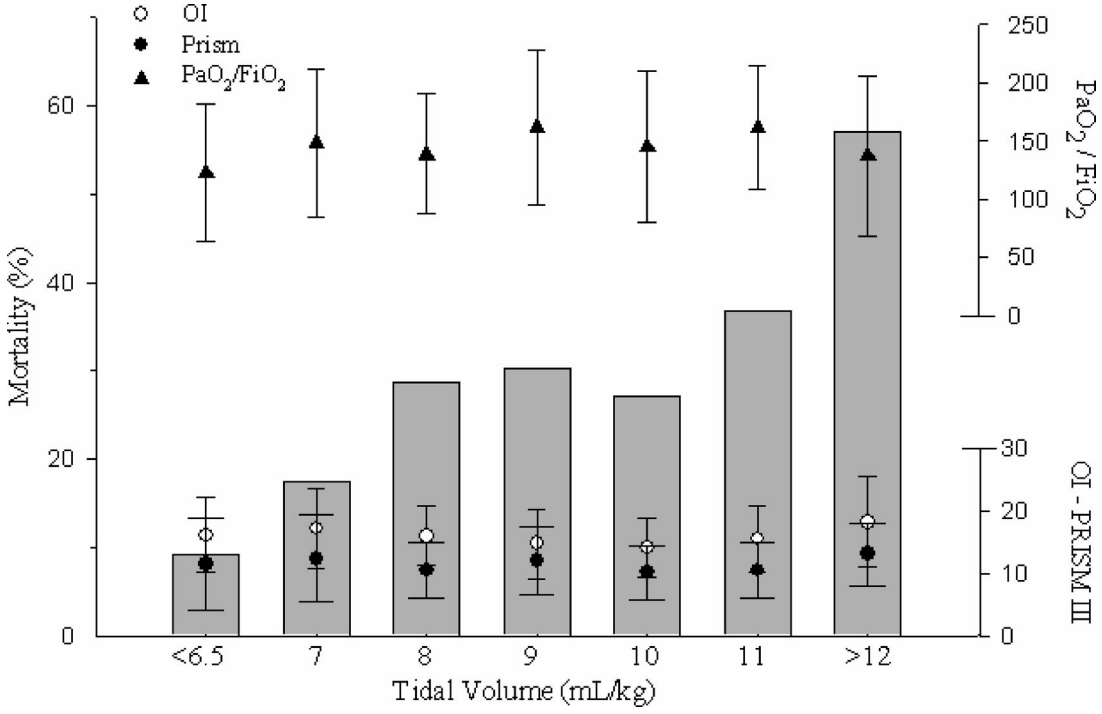

Figure 2. Mortality rate according to administered tidal volumes for actual body weight. Patients were divided into seven groups according to mean tidal volume received during the first 3 days. Tidal volume labels on the x-axis refer to limited ranges (i.e., 7 = 6.5–7.49). Mean oxygenation index (*OI*), baseline Pediatric Risk of Mortality (*PRISM*) III score, and Pao_2/Fio_2 were not significantly different.

1988–1992), we would better control for the bias associated with the generalized improvement in patient care. However, differences between groups might not have been detected because the transition to more protective strategies of ventilation (e.g., limiting of PIP, Vt, permissive hypercapnea) had already started to be implemented in adult critical care from the early 1990s (30, 44, 45).

Second, it is possible that the true Vt administered to patients was lower than the reported Vt. The Vt in this study represents the expiratory volume as measured by the ventilator, which could potentially be influenced by the compliance of the ventilatory circuit and circuit setup (46, 47). This is more relevant in neonates and infants when a relatively low Vt is being delivered (48). However, as the magnitude of Vt overestimation by the Siemens 300 (Siemens-Elema, Solna, Sweden) used in the recent group (46, 47) is similar to the Siemens 900 ventilator used in the past group (48), the difference detected in Vt administered between groups is expected to remain the same.

Third, the Vt reported is Vt per ABW instead of the more clinically relevant Vt per PBW. However, as the deviation of ABW from PBW is not expected to be significantly different between the two groups, the difference in Vt administered between groups is expected to remain the same.

While it is difficult to interpret retrospective data for prognostic values or cause-effect relationships, there are serious epidemiologic (49) and ethical limitations that make it difficult to conduct a prospective clinical trial designed to compare nonprotective and protective strategies of ventilation in pediatric patients.

The major strengths of this study are that 1) it is the first study to demonstrate that changes have occurred over time in the practice of MV in pediatric patients with ALI; 2) these changes follow the same trend as those described in adult critical care; and 3) it is apparently the first study to demonstrate a relationship between mortality and Vt in pediatric patients. Thus, a protective strategy of ventilation is applicable in pediatric patients, and there is an apparent positive impact of a limited Vt strategy on survival.

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