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Variability in usual care mechanical ventilation for pediatric Acute Respiratory Distress Syndrome: Time for a decision support protocol?

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Abstract

Objective—Although pediatric intensivists philosophically embrace lung protective ventilation for Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS), we hypothesized that ventilator management varies. We assessed ventilator management by evaluating changes to ventilator settings in response to blood gases, pulse oximetry or end tidal CO₂. We also assessed the potential impact that a pediatric mechanical ventilation (MV) protocol adapted from NHLBI ARDSNet protocols could have on reducing variability by comparing actual changes in ventilator settings to those recommended by the protocol.

Design—Prospective observational study.

Setting—Eight tertiary care US PICUs, October 2011 – April 2012.

Patients—120 patients (age range 17 days to 18 years) with ALI/ARDS.

Measurements and Main Results—2100 arterial and capillary blood gases, 3964 SpO₂ and 2757 PETCO₂ values were associated with 3983 ventilator settings. Ventilation mode at study onset was Pressure Control (PC) 60%, Volume Control (VC) 19%, Pressure-regulated Volume Control (PRVC) 18%, High Frequency Oscillatory Ventilation (HFOV) 3%. Clinicians changed FiO₂ by ± 5 or $\pm 10\%$ increments every 8 hours. PEEP was limited at ~ 10 cmH₂O as oxygenation worsened, lower than would have been recommended by the protocol. In the first 72 hours of MV, maximum tidal volume/kg using predicted versus actual body weight was 10.3 ml/kg; 8.5–12.9 (median; IQR) versus 9.2 ml/kg; 7.6–12.0 (p<0.001). Intensivists made changes similar to protocol recommendations 29% of the time, opposite the protocol's recommendation 12% of the time and no changes 56% of the time.

Conclusions—Ventilator management varies substantially in children with ARDS.

Opportunities exist to minimize variability and potentially injurious ventilator settings by utilizing a pediatric mechanical ventilation protocol offering adequately explicit instructions for given clinical situations. An accepted protocol could also reduce confounding by MV management in a clinical trial.

Keywords

Acute Lung Injury; Pediatric Acute Respiratory Distress Syndrome; Clinical Protocols; Decision Support Systems; Clinical; Pediatrics; Critical Care; Intensive Care; Conventional Mechanical Ventilation; High Frequency Oscillatory Ventilation

Introduction

Ventilator management for children with Acute Lung Injury and Acute Respiratory Distress Syndrome (now known collectively as Pediatric ARDS or PARDS) is suspected to vary between institutions(1) and between pediatric intensivists(2). Clinicians treating adults generally accept NIH/NHLBI ARDS network (ARDSNet) ventilator protocols(3) which have improved outcomes(3–5), but protocol implementation is not yet widespread(6;7). Few ventilator protocols exist for pediatrics although studies of ALI in children(8–10) have used protocols described as similar to ARDSNet protocols(3).

Protocols developed in the adult intensive care unit (ICU) may need modification for the pediatric ICU (PICU)(11). Pediatric intensivists commonly use different modes of mechanical ventilation (MV) than adult intensivists. There are unanswered questions including the magnitude of changes to fraction of inspired oxygen (FiO_2) and PEEP, and the acceptable range of permissive hypercapnia(11). Hence, we modified the ARDSNet protocol tables to develop a pediatric ARDS mechanical ventilation protocol(2;12).

In the 8 PICUs of the Collaborative Pediatric Critical Care Research Network (CPCCRN), we sought to determine “usual care” ventilator management practices in ALI/ARDS not guided by a protocol and to ascertain the potential applicability of our pediatric MV protocol. We hypothesized that there would be wide variability in usual care practice and inconsistency in MV decisions. We implemented a prospective, observational study to determine the frequency and scale at which intensivists changed ventilator settings. We compared these decisions against those recommended in our MV protocol to determine if use of the protocol could potentially decrease variability and increase more conservative decision making for similar clinical situations.

Methods

(For detailed Methods, see Supplemental Digital Content-Methods)

Institutional Review Board approval with waiver of consent was obtained for each site and the Data Coordinating Center (DCC). Eligibility criteria were MV via an endotracheal tube or tracheotomy; and three of the four diagnostic criteria for ALI/ARDS (acute onset of disease, at least two consecutive $\text{PaO}_2/\text{FiO}_2$ (P/F) ratios < 300 or two $\text{SpO}_2/\text{FiO}_2$ (S/F) ratios < 260 within 12 hours of initiation of ventilation, and no left ventricular dysfunction). The fourth criterion is bilateral infiltrates on chest film but this was not used for inclusion because of perceived subjectivity and inter-observer variability(13). Exclusion criteria were heart failure; uncorrected cyanotic heart disease; an endotracheal tube (ETT) leak $> 20\%$ (the difference between inspired and exhaled VT, measured at the ETT with a pneumotachometer); a lack of volume, pressure and flow measurements at the ETT, or the patient was receiving extracorporeal membrane oxygenation therapy.

Data was collected from October 2011 through April 2012 from 15 patients at each site). During this time there were no targeted mechanical ventilation strategies in place at any of the participating PICUs(14).

Data extraction

The first P/F ratio < 300 or S/F ratio < 260 after mechanical ventilation through an ETT or tracheotomy defined the beginning of the study for each patient. We extracted from the medical record blood gas values at least four times daily along with ventilator changes. We collected data for seven days or until extubation or death (whichever was first). S/F ratios were included only if the SpO₂ values were <98% (15). We associated ventilator settings with blood gas values based on time stamps. We analyzed patients supported by all conventional ventilation (CV) modalities (PC, VC, PRVC) and HFOV.

Pediatric ALI/ARDS mechanical ventilation protocol

Our pediatric ALI/ARDS mechanical ventilation protocol for conventional modes was modified from ARDSNet protocol tables (3) using preliminary data and expert review by intensivists from CPCCRN and the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) network. The HFOV protocol was based on a protocol developed in adults (16) where increasing amplitude rather than decreasing frequency is promoted as the lung protective strategy in situations of significant acidosis.

The protocol contains decision tables that implement ventilation strategies through discrete, explicit steps. Oxygenation tables evaluate combinations of positive end-expiratory pressure (PEEP) (or mean airway pressure – MAP - in the case of HFOV) and FiO₂ stratified into high, mid and low oxygenation (PaO₂ and SpO₂) subsets. The adult protocol tables are based on FiO₂ increments of 0.1; this was reduced to 0.05 (see Figure 1 for conventional modes and Figure 2 Supplemental Digital Content for HFOV mode).

Ventilation tables describe combinations of ventilator support, stratified by pH, for the different modes of CV. When pH is < 7.30, additional stratification is based on ventilator rate (VR, breaths/min, BPM). Pediatric intensivists recommended 25 BPM as a stratification point (compared to 35 BPM in the ARDSNet protocol). The protocol for PC mode (the predominant one used in this study) is shown in Table 3, Supplemental Digital Content.

Data preparation and comparison to the mechanical ventilation protocol

We used the pediatric MV protocol to group data for analysis. Combinations of blood gas and ventilator data ranges define data bins with a treatment recommendation. Data were entered into a secure electronic data capture system (OpenClinica®, Waltham, MA) maintained at the DCC (University of Utah, Salt Lake City, UT). We compared the protocol recommendations to the actual clinical care changes.

We used descriptive statistics to analyze initial blood gas and ventilator settings, times between PEEP and FiO₂ changes, transfers between CV and HFOV, and the variability of usual care regarding oxygenation and ventilation modes. Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Gary, NC).

Results

We analyzed 3,983 ventilator settings from 120 patients (age range 17 days to 18 years with no preterm infants), and were able to associate ventilator settings with 1,943 ABG, 157

CBG, 3,964 SpO₂ and 2,757 PETCO₂ values (Table 1). All patients met 3 of the 4 criteria for Acute Lung Injury (ALI) and 62% of the patients had bilateral pulmonary infiltrates (meeting all four ALI criteria) reported at some stage of their illness. Only 38% had quadrants of infiltrates described in radiology reports. On study entry the median P/F ratio was 128 and the S/F ratio was 162. The PALICC criteria for PARDS were devised after our study was performed. However, of the 120 patients enrolled, in the first 24 hours of mechanical ventilation, 87 had an OI $\geq$ 4 or OSI $\geq$ 5, thus meeting the new criteria. Ventilation mode at study onset was PC 60%, VC 19%, PRVC 18% and HFOV 3%. Overall mortality was 13.3%; the median length of mechanical ventilation was 6.5 days; the median number of 28-day ventilator-free days was 19.4 days (Table 1).

Initial blood gas and ventilator settings are described in Table 2 and the extent of changes and times between PIP, VT, PEEP and FiO₂ settings are shown in Table 3. The median time difference from blood gas to ventilator setting being recorded was 37 minutes. Descriptive statistics of the numbers of increases and decreases of FiO₂ and PEEP (all conventional modes) during selected study days are delineated (Supplemental Digital Content-Table 1). On conventional ventilation modes (PC, VC & PRVC), the median interval between ventilator changes was 4 hours.

The variability of usual care regarding oxygenation was examined with box plots of PEEP stratified by FiO₂ (Figure 1). The PC mode was used for 51% of observations. In order to evaluate variability in ventilation, we calculated the direction of changes to either PIP or VR after a blood gas for each of the 18 data bins in the PC ventilation table (Supplemental Digital Content-Table 2) as well as concordance of clinical care with what the protocol would have recommended (Supplemental Digital Content-Table 3).

Changes in FiO₂ and PEEP on Conventional Ventilation Modes

FiO₂ was changed a median of once per day on Days 1, 2, 3 and 7 (Supplemental Digital Content-Table 1) with the most common step size being $\pm$ 0.05, followed closely by $\pm$ 0.1 (Table 3). For patients in whom FiO₂ was changed more than once per day, the median time between FiO₂ changes was $\sim$ 4 hours (Table 3). The mean highest PEEP was 9.2 cmH₂O. No change in PEEP was made for most patients on any given study day (Supplemental Digital Content-Table 1). When changed, the most common alteration was $\pm$ 1 cmH₂O followed by $\pm$ 2 cmH₂O (47% and 41% of all PEEP changes, respectively).

Regardless of the PaO₂ or SpO₂ range (high, middle, low), clinicians were more likely to change FiO₂ than PEEP, resulting in considerable variability in the amount of FiO₂ used across different levels of PEEP (Figure 1). Clinicians used higher FiO₂ and lower PEEP than the protocol would have recommended, particularly when FiO₂ exceeded 0.6. When FiO₂ was 0.6 or less, the PEEP level generally corresponded with the protocol (Figure 1).

Changes in PIP and Ventilator Rate

For all modes of conventional ventilation, PIP was $\geq$ 35 cmH₂O in 92% of observations and 99% were $\geq$ 40 cmH₂O. Median VR was 20 BPM and 70% of values were $<$ 25 BPM with 4% $>$ 35 BPM.

When comparing ventilator settings to the PC protocol, there was a median of 21 (IQR 11, 50) observations per cell (Supplemental Digital Content-Table 2). Clinician response varied within each cell, with intensivists most commonly making no change (median 56.2% IQR 46.2, 58.5) (Supplemental Digital Content-Tables 2 and 3). This was true even when the PIP was > 35 cmH₂O, and the pH was > 7.45 (46%) or between 7.30–7.45 (62%). Forty-three per cent (466) of the 1091 observations had a PIP > 28 cmH₂O (with 17% being above 35 cmH₂O). The ventilator protocol would have recommended reducing the PIP in 72% of these scenarios but in practice PIP (or VR) was decreased in only 25%. In most cases no change was made and in 14% the PIP was actually increased.

Using a VR of >25 BPM to assign cells, intensivists made changes similar to protocol recommendations 29% of the time, opposite the protocol's recommendation 12% of the time and (in contrast to the program's recommendation) no changes 56% of the time.

Changes in Exhaled Tidal Volume

The mean exhaled VT at study entry was 7.4 ml/kg actual body weight (ABW) (Table 2). Over the course of ventilation, the VT averaged 7.1 (5.9, 8.4) ml/kg ABW (median, IQR). For PC mode, VT was 7.2 (5.7, 9.0), and for VC and PRVC modes together it was 7.1 (6.0, 8.0) ml/kg. Across all patients on CV modes, the median (IQR) VT was 7.3 (6.0, 8.5) ml/kg ABW.

There were 80 patients (66.7% of total) where both height/length and weight were recorded and for whom a PBW could be calculated (Relcore Inc, Los Angeles, CA). One PICU used ulna length (17;18) for height prediction where the child had contractures or marked scoliosis. Using PBW resulted in higher tidal volumes (VT/kg) than ABW ($p < 0.001$), irrespective of whether the highest (9.2; 7.6, 12.0 ml/kg ABW vs. 10.3; 8.5, 12.9 ml/kg PBW) or lowest (5.1; 4.0, 6.5 ml/kg ABW vs. 5.8; 4.2, 7.1 ml/kg PBW) [median; IQR] tidal volume was utilized.

Inter-site variability in conventional ventilator management

To assess how sites embraced permissive hypercapnia, we examined the subset of patients managed with PC ventilation who had severe ARDS (P/F ratio < 100 or S/F ratio < 150). When plotting the pH, PIP, and VT (Figure 2) on Days 1, 2, 3 and 7, there was a progressive decline in PIP, an increase in pH, and consistency of VT at approximately 7.5 ml/kg over the first 3 days. By Day 7, the VT had risen to ~ 11 ml/kg. When stratifying by site (Supplemental Digital Content-Figure 1) there was wide variation in pH values with similar PIP values and vice versa. At least one site was significantly different from another in the application of PIP, pH and VT/kg (Kruskal-Wallis test $p < 0.001$ for each).

We examined the pattern of Ventilation Index (VI) with either VR or PIP change. There was a modest increase in VI when pH was below 7.40. VI did not change between pH 7.40 to 7.55 then decreased again as the pH rose above 7.55. These differed from the CPCCRN protocol which recommends no change in VI for pH range 7.30 – 7.45 and a decrease in VI at pH > 7.45 .

Changes on High Frequency Oscillatory Ventilation Mode

Four patients (3.3%) began the study on HFOV mode with a further 13 patients (10.8%) switching to it during the study. Ten of the seventeen patients switched back to conventional modes. There were 444 recordings of HFOV ventilator settings with the most frequent decision being “No Change”. The distribution of MAP with FiO_2 is shown in Supplemental Digital Content-Figure 2. The last settings before changing modes between CV and HFOV and back are shown in Supplemental Digital Content-Tables 4A and 4B.

Discussion

This analysis demonstrated that intensivists, faced with children in similar states with ALI/ARDS, are inconsistent in their decisions about ventilator support. Most notably, clinicians did not decrease FIO_2 when the PaO_2 or SpO_2 was in a high range. Intensivists used low levels of PEEP and high levels of FiO_2 when PaO_2 and SpO_2 were low. This appears consistent with earlier reports(2;19). Furthermore, high peak pressures and ventilator rates were frequently not decreased, even when the pH was >7.45 (see Supplemental Digital Content-Figure 1).

We used our pediatric MV protocol to examine variability in clinician decision-making. We evaluated the potential ability of the protocol to reduce any such variability by comparing actual changes to changes the protocol would have recommended given the same patient state. We evaluated the direction, but not size, of change. If the protocol is actually representative of best available evidence then times when clinician responses differed from protocol recommendations might represent missed opportunities to improve lung protective ventilation practices. All protocols must allow for the fact that higher pressures and volumes do occur in clinical practice and the protocols should suggest a pathway to wean a patient safely back to more protective settings. The protocol will recommend increasing PIP above 28 cmH₂O only if the pH is < 7.15 . The PIP is never escalated above 35 cmH₂O. Our data showed PIP was escalated above 28 cmH₂O in 43% of the 1091 observations. The ventilator protocol would have recommended reducing the PIP in 72% of these scenarios but in practice it was done in only 25%. Hence, the recommendations of the protocol appear to decrease pressures more consistently than observed practice.

This pediatric MV protocol has not yet been formally validated against clinically important outcomes such as ventilator-free days or mortality. Its actual benefits are unknown, and validation studies are needed(20).

Prior to prospective studies, the protocol must first be acceptable to intensivists(21). From our analysis, the behavior of intensivists was directly contradictory to the protocol's recommendations only 12% of the time. This relatively low rate of direct contradiction suggests the protocol is, in general, consistent with current practice and likely acceptable to pediatric intensivists. Clinicians could have been responding to changes in continuous SpO_2 or PETCO_2 measurements rather than blood gases, as pulse oximetry and capnography were routinely used. Future studies should consider continuous ventilator, SpO_2 and PETCO_2 data collection techniques so that these apparent contradictions can be evaluated.

We identified a need to refine certain protocol recommendations such as the ventilator rate stratification at 25 BPM. In the adult protocol, this was intended to apply to a limited number of decisions where the patient was severely ill and aggressive change was needed. Pediatric intensivists escalated ventilator rate above 25 BPM in 28% of cases though only 4% of the time above 35 BPM. Perhaps the original cut off of 35 BPM is appropriate for pediatrics as well. This may also be the case for our reduction of FiO_2 step changes to 0.05, as many pediatric physicians appeared comfortable with 0.1 changes.

Another potential contributing factor to variability in ventilator settings is determining which weight should be used to standardize measurements related to mechanical ventilation (e.g., tidal volume, compliance and VT). In a recent study of 325,325 PICU patients' height was recorded only 39% of the time(22). In our study it appeared that ABW was used to calculate exhaled VT and other variables, since height was recorded in only two-thirds of cases. There was a wide variation of exhaled VT and a median of 1.3 ml/kg above the low VT target (6 ml/kg) in the ARDSNet study(3). Ward et al(23) undertook a retrospective data analysis from ARDS patients amalgamated from 4 studies and found underutilization of low tidal volumes, particularly in overweight children, in the first 24 hours. Our prospective study confirms and expands the finding over 7 days. Additionally, VT as measured in some ventilators is lower than the real volume(24). Investigation of measured lung volumes, compared to those calculated from ABW versus PBW in children, and whether the PBW use has an effect on pediatric ARDS outcomes, is a priority(25). Provocatively, a recent meta-analysis (26) suggested that unlike the ARDSNet trial in adults, VT is not associated with mortality in pediatrics.

In this study only 17 (14.2%) patients were placed on HFOV. This is consistent with earlier observations(1;27–29) that HFOV is used only in about 10% of children with ARDS and reinforces the view that pediatric HFOV is reserved as a “rescue” modality for patients failing conventional ventilation. In our study, it appeared that once a patient stabilized, little change was made to any HFOV parameter save for inspired oxygen. Since variability seems less of an issue in HFOV mode it may be that using decision support tools such as ours could decrease pressures more quickly and consistently with even less potential for lung injury.

The adult Berlin(30) and Pediatric Acute Lung Injury Consensus Conference (PALICC)(31) definitions of ARDS require the presence of bilateral or new pulmonary infiltrates, respectively, on chest radiograph and the pLIS(32;33) requires quadrants of disease. The low incidence of reporting of these abnormalities questions the relevance of this information in the scoring systems, although it is possible that intensivists read the films directly rather than relying on radiology reports.

Some may consider it a limitation that we analyzed PIP rather than Plateau Pressures. However, in the CPCCRN group pressure-regulated modes (PC or PRVC) were most commonly used. Given the differing flow profile of delivered gas in these modes from VC, Pplat and PIP are nearly always the same except in circumstances of significant elevations in airway resistance. Given these patients had pediatric ARDS, previous studies have shown that is not expected(34;35).

Our analysis has limitations in that we could not elucidate the reasons for clinician decisions with respect to ventilator or oxygenation changes. It is possible that intensivists used data outside of the parameters in the ventilator protocol (i.e. such as hemodynamic variables or work of breathing) in their decisions to change or not change ventilator settings. It is also possible that the CPCCRN group of PICUs may not be representative of either American or international practice. However, the clear trends and consistent findings from a large number of observations from over 50 critical care physicians in 8 PICUs give strength to our conclusions. In addition, the publication of the PALICC guidelines in June 2015(31) subsequent to our study may also have begun to reduce variability even without the aid of a specific protocol.

Conclusions

Although pediatric intensivists have philosophically embraced lung protective ventilation for children with ARDS, ventilator management varies substantially with many apparent lost opportunities to minimize potentially injurious ventilator settings. An accepted ventilator management protocol(20) might encourage less variability and more systematic decisions about reductions in pressures and volumes. However, a randomized, controlled trial is needed to determine if adherence to such a protocol leads to a better outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Box Plot of PEEP/FiO₂ combinations on all patients on conventional ventilation modes in the 8 CPCCRN PICUs.

PEEP/FiO₂ titration tables from clinical care for all 120 patients on conventional modes of mechanical ventilation. The Y-axis represents actual PEEP values as a function of actual FiO₂ used (X-axis). The superimposed dark blue boxes represent the pediatric mechanical ventilation protocol target combinations of PEEP/FiO₂, derived from the ARDS Network protocols. For all patients, there is variability in PEEP/FiO₂ combinations intensivists choose. In general, clinicians use less PEEP (peaking at just under 10 cmH₂O) than the protocol would recommend, particularly when FiO₂ climbs above 0.6.

- Actual CPCCRN data (Light blue boxes); Mean value (◇), Median (Bar), IQR (Box), Range (Whiskers), Outliers (O), Protocol Targets (Dark blue bars).
- Missing values are for 15 of the 3504 PEEP/FiO₂ observations for which no FiO₂ was recorded. In addition, there were 26 observations excluded where no PEEP was recorded.

CPCCRN Sites 1 - 8

Figure 2.

The distribution of Peak Inspiratory Pressure (PIP), pH and Tidal Volume/kg actual body weight averaged for all 8 CPCCRN sites over Days 1, 2, 3 and 7 when treating patients with severe ARDS – PF ratio < 100 or SF ratio < 150.

The Y-axis on the left shows the PIP (upper) and the VT (mL/kg) (lower) values and on the right, the pH values over the first 3 days of MV and Day 7, for all CPCCRN sites and all patients with severe ARDS.

- Tidal volumes were maintained in the 7–8 mL/kg range for this group of patients with severe pediatric ARDS over the first three days. The resolution of disease over the week is implied by decreasing peak pressures and rising pHs with tidal volumes having increased up to approximately 11 mL/kg ABW.
- Mean value (◇), Median (Bar), IQR (Box), Range (Whiskers), Outliers (○).

Table 1

Demographics and Outcomes of Patients

Variable	Count	%	Median	IQR
Gender (Male)	61	50.8		
Age (years)	120	100.0	2.0	0.5, 9.0
Weight (kg)	120	100.0	11.5	6.3, 29.6
Height (cm)	82	68.3	80.5	59.0, 112.0
Race				
White	64	53.3		
Black	29	24.2		
Other	27	22.5		
Ethnicity				
Hispanic or Latino	23	19.2		
Not Hispanic or Latino	53	44.2		
Unknown	44	36.7		
Chest films	618	100.0		
Patients with no report of Bilateral infiltrates	46	38.3		
Patients with no report of Quadrant infiltrates	74	61.7		
Number Ventilator records	3983			
Number Ventilator changes	3863			
Arterial Blood Gases (ABG)	1943			
Patients with ABG	88	73.3		
Capillary Blood Gases (CBG)	157			
Patients with CBG	27	22.5		
Number SpO2 records	3964			
Number PETCO2 records	2757			
Mortality (Died)	16	13.3		
Length Mechanical Ventilation (d) **	113 *	94.2	6.5	3.5, 11.5
28 Day Ventilator-free days	120 δ	100	19.4	8.6, 23.4

* excludes 7 patients discharged on mechanical ventilation.

δ includes data from the 16 dead patients (assumes VFD = 0)

** Non-invasive ventilation not included.

Table 2

Descriptive statistics of initial ventilator settings and blood gases obtained within 6 hours following study entry

Variable	Count	%	Median	IQR
PF O ₂ ratio	37		128.3	94.0, 211.4
SF O ₂ ratio	60		162.0	115.2, 228.8
Oxygenation Index	29		12.0	7.9, 18.1
Oxygenation Saturation Index	36		7.9	4.8, 12.5
PEEP (cmH ₂ O)	115		7.0	5.0, 10.0
PIP (cmH ₂ O)	115		27.0	23.0, 32.0
MAP (cmH ₂ O)	82		13.0	11.0, 16.0
VT exhaled (ml/kg) *	110		7.4	6.0, 8.5
Ventilator Rate (BPM)	116		24.0	20.0, 30.0
FiO ₂	116		0.6	0.4, 0.8
pH	45		7.31	7.21, 7.36
Part & Pcap CO ₂ (mmHg)	45		43.3	38.4, 48.0
PETCO ₂ (mmHg)	70		38.0	31.0, 48.0
Ventilator Modes				
Pressure Control (PC)	72	60.0		
Volume Control (VC)	23	19.2		
Pressure Regulated Volume Control (PRVC)	21	17.5		
High Frequency Oscillatoy Ventilation (HFOV)	4	3.3		

All ventilation modes excluding HFOV - some missing values, particularly SF O₂ ratios after study entry where SpO₂ > 97%.

* Exhaled tidal volume measured at the endotracheal tube. This value was then divided by actual body weight to report tidal volume (V_T ml/kg).

Table 3

Magnitudes of changes and Times between increases and decreases of FiO₂ and selected ventilator settings for conventional modes

Variable	Count	Median	IQR
Time between Ventilator Settings (h)			
Time between FiO ₂ increases (h)	431	4.5	2.0, 11.8
Extent of FiO ₂ increases	431	0.10	0.05, 0.2
Time between FiO ₂ decreases (h)	799	3.8	1.6, 7.3
Extent of FiO ₂ decreases	799	-0.10	-0.10, -0.05
Time between PEEP increases (h)	173	5.5	1.9, 14.9
Extent of PEEP increases (cmH ₂ O)	173	2.0	1.0, 2.0
Time between PEEP decreases (h)	285	10.5	4.5, 21.5
Extent of PEEP decreases (cmH ₂ O)	285	-1.0	-2.0, -1.0
Time between PIP increases (h)	685	4.2	2.3, 7.0
Extent of PIP increases (cmH ₂ O)	685	2.0	1.0, 5.0
Time between PIP decreases (h)	906	4.1	2.2, 7.4
Extent of PIP decreases (cmH ₂ O)	906	-2.0	-4.0, -1.0
Time between Tidal Volume increases (h)	898	4.1	2.5, 6.6
Extent of Tidal Volume increases (ml/kg)	898	0.8	0.4, 1.6
Time between Tidal Volume decreases (h)	955	4.0	2.4, 6.6
Extent of Tidal Volume decreases (ml/kg)	955	-0.8	-1.5, -0.4
Time between Ventilator Rate increases (h)	222	5.3	2.4, 12.0
Extent of Ventilator Rate increases (BPM)	222	4.0	2.0, 8.0
Time between Ventilator Rate decreases (h)	565	7.0	3.3, 15.0
Extent of Ventilator Rate decreases (BPM)	565	-4.0	-5.0, -2.0