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Ventilator Settings in Critically Ill Pediatric Patients (VESPer)—insights from a European Registry

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Abstract

Aim To explore ventilator settings, ventilation variables and parameters in critically ill pediatric patients across European Centers.

Methods International, multicenter, prospective observational study, collecting ventilation data for 7 days from patients aged ≤ 12 years, requiring ventilatory support for ≥ 12 h. Primary endpoint was a set of key ventilator settings, including tidal volume (V_T), respiratory rate (RR), peak and mean airway pressure (Ppeak and Pmean), positive end–expiratory pressure (PEEP), and the fraction of inspired oxygen (FiO_2). Ventilator settings were compared across neonates (aged < 1 month), infants (1 to 12 months), toddlers (1 to 3 years) and children (4 to 12 years), and between patients with and without pediatric acute respiratory distress syndrome (PARDS).

Results Patients enrolment occurred in 43 centers in 11 countries, with a total of 166 patients—mostly infants—included in this analysis. The majority began with invasive ventilation, while one–third started with noninvasive ventilation (NIV) or high–flow nasal oxygen (HFNO). Patients on invasive ventilation, NIV and HFNO were weaned within a median of 3 [2–6], 3 [2–4] and 3 [2–4] days, respectively. In 22% of patients, NIV or HFNO was used following invasive ventilation. V_T, RR and FiO_2 varied across age groups, and airway pressures were higher in PARDS patients.

Conclusions In this cohort, ventilator settings, and ventilation variables and parameters, varied between individual patients and across patient groups. Larger studies are needed to confirm this variability, explore associations between ventilation practices and clinical outcomes, and assess temporal and geo–economic differences.

Keywords Pediatric intensive care units, Invasive ventilation, Noninvasive ventilation, High–flow nasal canula, Ventilator settings

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Introduction

Critically ill pediatric patients frequently require ventilatory support, which, while lifesaving, carries inherent risks [1, 2]. Despite its critical importance, research on ventilatory support practices in this patient population remains notably limited. Historical studies have revealed considerable variability in key ventilatory support settings [3–14]. Lung–protective strategies in invasive ventilation may have become more prevalent, and advancements in noninvasive ventilation (NIV) and high–flow nasal oxygen (HFNO) may have shifted ventilatory support to these modalities [15–18]. Furthermore, ventilation practices in adult patients show significant variation across patient types [19–27] and geo–economic regions [28], and it can be expected that this variation also exists in children.

In adult patients, key ventilatory support variables and parameters, like tidal volume (V_T), positive end–expiratory pressure (PEEP) and other airway pressures, fraction of inspired oxygen (FiO_2), driving pressure (ΔP) and the mechanical power of ventilation (MP) have been shown to have associations with important outcomes like duration of ventilation and length of stay, and even mortality [19–27]. Similar associations may exist in critically ill pediatric patients, highlighting the importance of conducting studies that collect these data in much greater detail. Such research is essential to deepen our understanding of ventilation practices and their impact on clinical outcomes in pediatric critical care.

The 'Ventilator Settings in Critically Ill Pediatric Patients—a European Registry' (VESPer) study was conducted to systematically examine ventilator settings, as well as ventilatory variables and parameters, in critically ill pediatric patients across European centers. The study aimed to explore specifically the variability in ventilatory management practices among different patient groups of critically ill patients receiving either invasive or noninvasive ventilation. We hypothesized that ventilation practices would vary, both between individual patients and among distinct patient groups, potentially reflecting differences in underlying conditions, as well as treatment goals and institutional protocols.

Material and methods

Design

VESPer was an investigator–initiated, international, multicenter, prospective observational study. European centers were approached to collect data regarding ventilatory support in a predefined 2–week period from October 2015 to April 2016. The study protocol of VESPer was approved by the Institutional Review Board of the University Medical Center Groningen, the Netherlands (2015/187). Individual patient informed consent was waived because of the strict observational nature of this study.

Selection of centers

Centers were invited to participate in VESPer through a call issued by 'Respiratory Failure' section the 'European Society of Pediatric and Neonatal Intensive Care' (ESPNIC).

Inclusion and exclusion criteria

Upon confirmation of participation, local investigators screened patients in the predefined 2–week period. Patients were eligible for participation in VESPer if: (1) aged ≤ 12 years; (2) admitted to the Pediatric Intensive Care Unit (ICU) of a participating center; (3) starting on ventilatory support during the enrolment period which could begin with either invasive ventilation, NIV or HFNO; and (4) that was expected to last at least 12 h. Patients admitted to a neonatal or an adult ICU were excluded, as were patients that received ventilatory support because of a perinatal–related condition.

Data collected

Data collection included patient demographics and baseline characteristics, admission diagnosis, and disease severity scores. For seven days, starting from the day of initiation of ventilatory support, daily data were collected. Day 0 was defined as the day of initiation of ventilatory support. Day 1 to 7 represented ventilator settings in the morning between 6 and 9 am (essentially before the first morning blood gas was drawn and ventilator settings could be changed). Daily data was collected for a maximum of 7 days of ventilatory support. For patients receiving invasive ventilation, daily ventilatory support characteristics were recorded, including expiratory V_T, set and measured respiratory rate (RR), peak airway pressure (Ppeak), mean airway pressure (Pmean), plateau pressure (Pplat), PEEP, FiO_2, and inspiratory time. For patients on NIV, daily support characteristics included PEEP, pressure support (PS), Ppeak, RR, and FiO_2. For those receiving HFNO, data included air flow and FiO_2. Measures of oxygenation and decarboxylation were also collected, such as pulse oximetry oxygen saturation (SpO_2), end–tidal carbon dioxide ($etCO_2$), and results from arterial or capillary blood gas analyses, as well as the use of adjunctive therapies.

Definitions and calculations

Patients were categorized by age into neonates (aged < 1 month), infants (1 to 12 months), toddlers (1 to 3 years) and children (4 to 12 years). Pediatric acute respiratory distress syndrome (PARDS) was defined according to the 2015 'Pediatric Acute Lung Injury Consensus Conference' (PALICC) definition [29].

For calculation of static and dynamic airway pressure gradients and respiratory system compliance (C_{RS}), we used the following equations [1, 30]:

$$\text{static airway pressure gradient} = \text{Pplat} - \text{PEEP} \quad (1)$$

$$\text{dynamic airway pressure gradient} = \text{Ppeak} - \text{PEEP} \quad (2)$$

$$C_{RS} = V_T / (\text{Pplat} - \text{PEEP})(\text{in VCV}) \quad (3)$$

$$C_{RS} = V_T / (\text{Ppeak} - \text{PEEP})(\text{in PCV}) \quad (4)$$

Study endpoints

The primary endpoint was a set of key ventilator settings, including V_T, RR, Ppeak and Pmean, PEEP, and FiO_2. Secondary endpoints included other ventilatory support settings, and ventilatory variables and parameters.

Sample size calculation

We did not perform a formal sample size calculation. All results must be seen as explorative.

Statistical analysis

Descriptive statistics are used to describe patient demographics and baseline characteristics, types of ventilatory support, ventilator settings and ventilation parameters. Continuous variables are expressed in medians and interquartile ranges, categorical variables are expressed in frequencies and proportions.

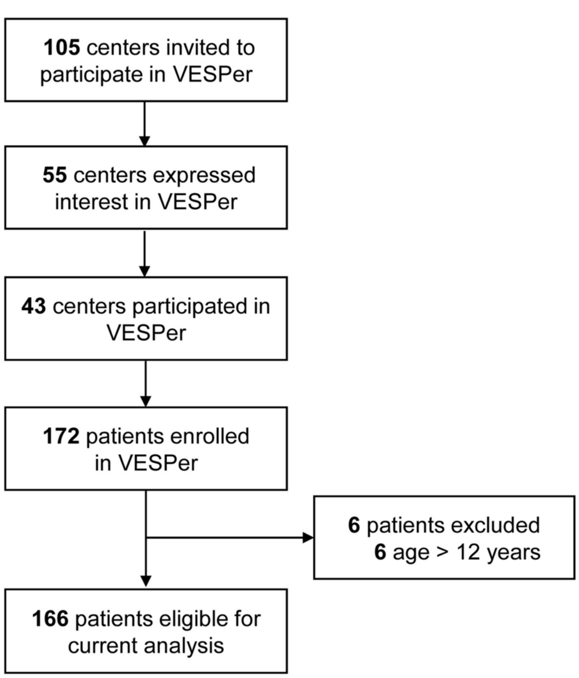

Fig. 1 CONSORT diagram. Patient flow in VESPer

Settings, variables and parameters were compared across the four age groups, and between patients with and without PARDS.

Cumulative distribution plots and line graphs are used to visualize the key ventilator settings.

Data are analyzed with R (R Core Team, 2022, Vienna, Austria, version 4.2.2). Statistical uncertainty is expressed by 95%–confidence levels. A P–value < 0.05 was considered statistically significant.

Results

Centers and patients

Of 105 centers invited to participate in VESPer, 55 initially expressed interest in participating (Fig. 1). Ultimately, 43 centers, 1 in Belgium, 1 in Finland, 7 in France, 1 in Italy, 4 in the Netherlands, 1 in Poland, 5 in Portugal, 13 in Spain, 1 in Switzerland, 4 in Turkey, 5 in United Kingdom included a total of 166 patients. Most patients were infants, and the most common reason for ventilatory support was a respiratory disease (Table 1). The prevalence of comorbidities amongst patients was high, with cardiac and pulmonary diseases being the most common. A minority of patients (10%) had PARDS.

Types of respiratory support

Two–thirds of the patients started with invasive ventilation, and most of them with a PCV mode (Fig. 2 and Table 2). In the other patients, half started with NIV and the other half with HFNO. Patients under invasive ventilation, NIV and HFNO were weaned within a median 3 [2–6], 3 [2–4] and 3 [2–4] days from the first modality of respiratory support, respectively. NIV or HFNO was used in 24 patients (22%) after weaning from invasive ventilation.

Respiratory support settings

In patients receiving invasive ventilation, median V_T and RR were 7 [6–9] ml/kg actual body weight (ABW) and 30 [24–36] breaths/min, respectively, with notable variations observed between different age groups (Table 2 and Fig. 3). Median Ppeak and Pmean were 21 [18–25] and 10 [9–13] cmH_2O, respectively, with higher pressures observed in PARDS patients compared to those without. Median PEEP and FiO_2 were 5 [5–6] cmH_2O and 45 [35–60] %, respectively, with higher values in PARDS patients compared to those without. Lung–protective ventilation with a $V_T < 8$ ml/kg was applied in 57% of the patients at day 0, the majority of the patients was ventilated with PEEP lower than 6 cmH_2O (70%) and peak pressures lower than 30 cmH_2O (87%). Key ventilatory variables remained stable over time during the initial days of ventilatory support (eFigure 1).

Table 1 Patient demographics and admission characteristics

	n = 166
Demographics	
Age (months), median [IQR]	9 [2 – 37]
Male, n (%)	91 (55)
Weight (kg), median [IQR]	9 [4 – 14]
Height (cm), median [IQR]	74 [57 – 98]
History of premature birth, n (%)	27 (16)
Admission category	
Medical unplanned, n (%)	101 (61)
Medical planned, n (%)	7 (4)
Surgical planned, n (%)	36 (22)
Surgical unplanned, n (%)	22 (13)
Admission diagnosis	
Respiratory, n (%)	75 (45)
Circulatory, n (%)	22 (13)
Neurological, n (%)	8 (5)
Metabolic, n (%)	2 (1)
Post-operative, n (%)	52 (31)
Trauma, n (%)	6 (4)
Comorbidities	
None, n (%)	84 (51)
Pulmonary, n (%)	20 (12)
Cardiac, n (%)	39 (23)
Neuromuscular, n (%)	3 (2)
Syndrome/genetic abnormalities, n (%)	18 (11)
Oncologic, n (%)	8 (5)
Organ transplant, n (%)	3 (2)
Chronic ventilation, n (%)	0 (0)
Mental retardation, n (%)	5 (3)
Type of ventilatory support at day 0	
Invasive ventilation, n (%)	111 (67)
NIV, n (%)	33 (20)
HFOV, n (%)	0 (0)
HFNO, n (%)	22 (13)
Severity score	
PRISM III	17 [13 – 20]
Blood gas results	
pH, median [IQR]	7.34 [7.27 – 7.40]
PaO_2 (mmHg), median [IQR]	84 [64 – 118]
$PaCO_2$ (mmHg), median [IQR]	41 [36 – 50]

Abbreviations: *HFNO* high flow nasal oxygen, *HFOV* high frequency oscillatory ventilation, *NIV* non-invasive ventilation, *PaO_2* partial arterial oxygen pressure, *PCO_2* partial pressure of carbon dioxide, *PRISM III* pediatric risk of mortality III score

In patients receiving NIV, median Ppeak, Pmean and PEEP were 11 [7–14], 8 [7, 8] and 7 [6, 7] cmH2O, respectively, and median FiO2 was 40 [30–50] %.

In patients receiving HFNO, median flow rate was 1 [1, 2] L/kg/min, and median FiO2 was 40 [40–50] %.

Respiratory support parameters

In invasively ventilated patients, median static and dynamic respiratory system compliance was 6 [4–9] and 4 [2–10] mL/cmH_2O respectively; median static and dynamic airway pressure gradient was 12 [9–16] and 15 [12–18] cmH_2O. Static and dynamic respiratory system compliance was notably higher in older children, while static and dynamic airway pressure gradient was lower in older children (eTable 1).

Gas exchange parameters

Median $etCO_2$ was 36 [30–41] mmHg and median SpO_2 was 98 [95–100] %. In patients with capillary or arterial blood gases performed, median pH was 7.3 [7.3–7.4], median pO_2 was 84 [64–118] mmHg, and median pCO_2 41 [36–50] mm Hg. Higher pO_2 levels were observed in older children (eTable 1) and those without PARDS compared to PARDS patients (eTable 2).

Adjunctive therapies

Patients received adjunctive respiratory therapies, including nitric oxide (4%), steroids (24%), neuromuscular blocking agents (16%), and prone positioning (6%). Nitric oxide and neuromuscular blocking agents were used more often in younger children, while steroids were more common in older children (eTable 1).

Discussion

This report describes ventilation practices in critically ill pediatric patients receiving ventilatory support for at least 12 h. The main findings were (1) that there is substantial variability in the types of ventilatory support used; and (2) that key ventilator settings, as well as ventilation variables and parameters vary among patient groups.

VESPer has several strengths. We contacted centers through a call issued by the leading ESPNIC, which helped us identify major European centers that might be interested in participating in a larger study on this topic. A total of 43 different centers in 11 countries participated, increasing the generalizability of the findings. Detailed information on ventilator settings and parameters were captured. Furthermore, we collected data during various seasons, and in various patient groups, with complete data available for most patients, allowing for a robust analysis.

The findings of our study can be compared with similar studies in adults, such as the 'Large observational study to UNderstand the Global impact of Severe Acute respiratory FailurE' (LUNG SAFE) [31], 'PRactice of VENTilation in critically ill patients without ARDS at onset of ventilation' (PRoVENT) [32], and 'PRactice of VENTilation in Middle–income Countries' (PRoVENT–iMiC) [33]. These studies have significantly contributed to shaping the research landscape within adult intensive care medicine. LUNG SAFE and PRoVENT provided crucial insights into ventilatory support practices and outcomes, identifying areas where further research was needed.

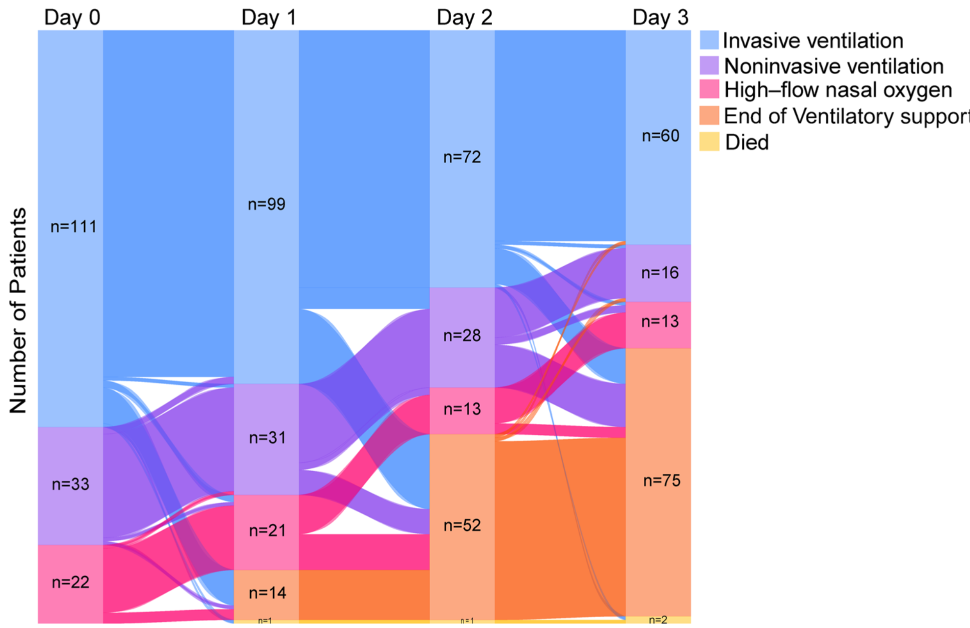

Fig. 2 Alluvial plot illustrating the types of ventilatory support used in the first days in ICU, including invasive ventilation, noninvasive ventilation, and high–flow nasal oxygen, and their subsequent usage patterns. The blocks indicate the number of patients receiving ventilatory support at day 0, 1, 2 and 3. The stream fields between the blocks represent changes in ventilatory support over time

PRoVENT–iMiC expanded on this and demonstrated the feasibility of such studies in centers in Asian countries, paving the way for larger worldwide studies that include both centers in resource–rich and resource–limited settings. These studies found that certain ventilatory variables were associated with important clinical outcomes [19–27]. It is likely that similar associations exist in pediatric patients. Historical studies have found variability in key ventilatory support settings [3–14] and investigated some aspects of ventilation. A recent nonrandomized controlled trial found that lung protective ventilation strategies in patients with PARDS was associated with reduced mortality [34]. Additionally, studies in both adult and pediatric ICU patients suggest that ventilation practices evolve over time. For example, during the COVID-19 pandemic, studies in adults showed increased adherence to lung-protective ventilation protocols, with lower tidal volumes and more frequent use of prone positioning [35–37], compared to earlier ventilation practices [31, 32]. In pediatric patients, the COVID–19 pandemic also impacted on pediatric respiratory infections, with fewer PICU admissions in 2020–2021 [38, 39], followed by a resurgence with studies reporting higher disease severity and an increased need for mechanical ventilation [40–42]. These evolving trends underscore the need for ongoing research into the effects of ventilation strategies in critically ill children. We hope our findings will help establish a similar research landscape for critically ill children, akin to that in adult intensive care medicine.

Our findings reveal remarkable variability in ventilation practices. Various modes of ventilatory support were reported not only within invasive ventilation but also among the different types of respiratory support available. Interestingly, our data suggest a more frequent use of lung–protective ventilation with low V_T. Previous research has shown less consistent use of low V_T and considerable variability in V_T size [6, 9, 15]. The use of PEEP was generally consistent with other studies [3, 4]. Notably, our study was conducted after publication of guidelines by the Pediatric Acute Lung Injury Consensus Conference Group (PALICC) in 2015 [29]. These guidelines recommend using V_T within or below the physiological range of 5 to 8 ml/kg body weight and maintaining an inspiratory plateau pressure limit of 28 cmH_2O. They also recommend a PEEP of 10–15 cmH_2O for children with severe PARDS but do not provide specific recommendations for non-severe cases. In our cohort, only 10% of patients met the PARDS criteria, with most classified as mild and only 2% as severe. Among those with severe PARDS, the mean PEEP was higher than in patients without severe PARDS, averaging 10 cmH_2O. Similar to findings from the Paediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE) study, PEEP levels in clinical practice often remain lower than recommended by the Acute Respiratory Distress Syndrome Network PEEP/FiO_2 grid [43].

We found that one–third of the children initially received NIV or HFNO. This observation reflects a growing trend towards the more intensive use of noninvasive forms is ventilatory support [15–18, 44]. In particular, interest in HFNO is increasing in pediatric care, as it is often better tolerated than NIV. Emerging evidence

Table 2 Ventilatory characteristics at day 0

Invasive mechanical ventilation	***n*=111**
Mode of ventilation	
Pressure control, n (%)	51 (46)
Volume control, n (%)	15 (14)
Pressure support, n (%)	31 (30)
Volume support, n (%)	11 (10)
CPAP, n (%)	1 (1)
Ventilatory variables	
V_{Te} (ml/kg ABW), median [IQR]	7 [6 – 9]
< 6, n (%)	19 (16)
6–8, n (%)	44 (13)
8–10, n (%)	17 (15)
10–12, n (%)	13 (12)
> 12, n (%)	7 (6)
PEEP (cm H2O), median [IQR]	5 [5 – 6]
< 6, n (%)	78 (70)
6–8, n (%)	15 (14)
8–10, n (%)	8 (7)
10–12, n (%)	5 (5)
> 12, n (%)	2 (2)
Ppeak (cmH_2O), median [IQR]	21 [18 – 25]
Pmean (cmH_2O), median [IQR]	10 [9 – 13]
RR set (breath/min), median [IQR]	30 [24 – 36]
RR measured (breath/min), median [IQR]	33 [25 – 40]
FiO_2 (%), median [IQR]	45 [35 – 60]
Static C_{rs} (ml/cmH_2O), median [IQR]	6 [4 – 9]
Dynamic C_{rs} (ml/cmH_2O), median [IQR]	4 [2 – 10]
Static airway pressure gradient (cmH_2O), median [IQR]	12 [9 – 16]
Dynamic airway pressure gradient (cmH_2O), median [IQR]	15 [12 – 18]
Noninvasive ventilation	***n*=33**
Mode of ventilation	
Pressure control, n (%)	7 (21)
Pressure support, n (%)	14 (42)
CPAP, n (%)	6 (18)
Ventilatory variables	
PEEP (cm H_2O), median [IQR]	7 [6 – 7]
Ppeak (cm H_2O), median [IQR]	11 [7 – 14]
Pmean (cm H_2O), median [IQR]	8 [7 – 8]
FiO_2 (%), median [IQR]	40 [30 – 50]
High-flow nasal oxygen	***n*=22**
Flow rate (L/kg/min), median [IQR]	1 [1 – 2]
FiO_2 (%), median [IQR]	40 [40 – 50]

Abbreviations: *ABW* actual body weight, *CPAP* continuous positive airway pressure, V_{Te} expiratory tidal volume, FiO_2 fraction of inspired oxygen, *Pmean* mean airway pressure, PaO_2 partial arterial oxygen pressure, PCO_2 partial pressure of carbon dioxide, *Ppeak* peak pressure, *PEEP* positive end-expiratory pressure, *RR* respiratory rate, C_{RS} respiratory system compliance

shows that HFNO may be associated with reduced work of breathing, improved ventilatory support efficiency, and a decreased need for intubation in children with respiratory insufficiency compared to standard low flow oxygen therapy. This has been observed both in ICU settings [16–18, 45] and outside of them [46]. Two RCTs comparing HFNO with CPAP showed that HFNO, as a step-up strategy, was non-inferior to CPAP for time to liberation from respiratory support, with significantly lower use of sedation and lower duration of ICU stay in the HFNO group [47]. However, HFNO failed to show noninferiority to CPAP as a step-down strategy in children extubated after invasive mechanical ventilation [48]. Our reported rate of 22% for post-extubation use of NIV or HFNO appear lower than those in more recent trials [48, 49]. This discrepancy may be due to differences in study periods, as our data were collected in 2015/2016, whereas newer studies reflect evolving ventilation practices. Additionally, since our dataset captured ventilatory support only once per day, short-term NIV or HFNO use may have been underestimated.

In our study, the incidence of PARDS was higher compared to that reported in other studies [4, 50, 51]. One meta–analysis of studies in children found that the pooled weighted population-based incidence of 2 to 10 times lower than in adult studies in Europe and the US, respectively [51]. The lower incidence of PARDS in children might result from under recognition or underreporting, as interpreting bilateral radiographic infiltrates on chest radiography can be challenging [29]. However, PARDS might also be a different syndrome from adult ARDS, as mortality rates differ, and poor initial oxygenation predicts worse outcomes in PARDS but not in adult ARDS [52]. Larger studies, as well as studies specifically focused on PARDS, are needed to better understand its incidence and characteristics, especially regarding the way ventilatory support is provided.

In line with previous investigations of ventilation practices in adult patients, our data indicate that ventilator settings and ventilation parameters remain relatively stable over the initial days of support [28, 32]. This finding is significant because it suggests that the collection of these data, which can be very time-consuming, can be limited in future studies. This reduction in data collection effort would enhance the feasibility of conducting larger studies.

VESPer had several limitations. The willingness to participate may have introduced bias, as centers with a particular interest in ventilatory support may have been more likely to join. While data collection was nearly complete for most patients, we were unable to determine the total number of admitted patients and outcome data were missing for some centers. This may have been due to early transfers to other facilities, which made it difficult or impossible to gather this information. Future studies should strive for rigor and clarity to avoid this issue. Additionally, we did not have screening data to assess the proportion of eligible patients enrolled. The low

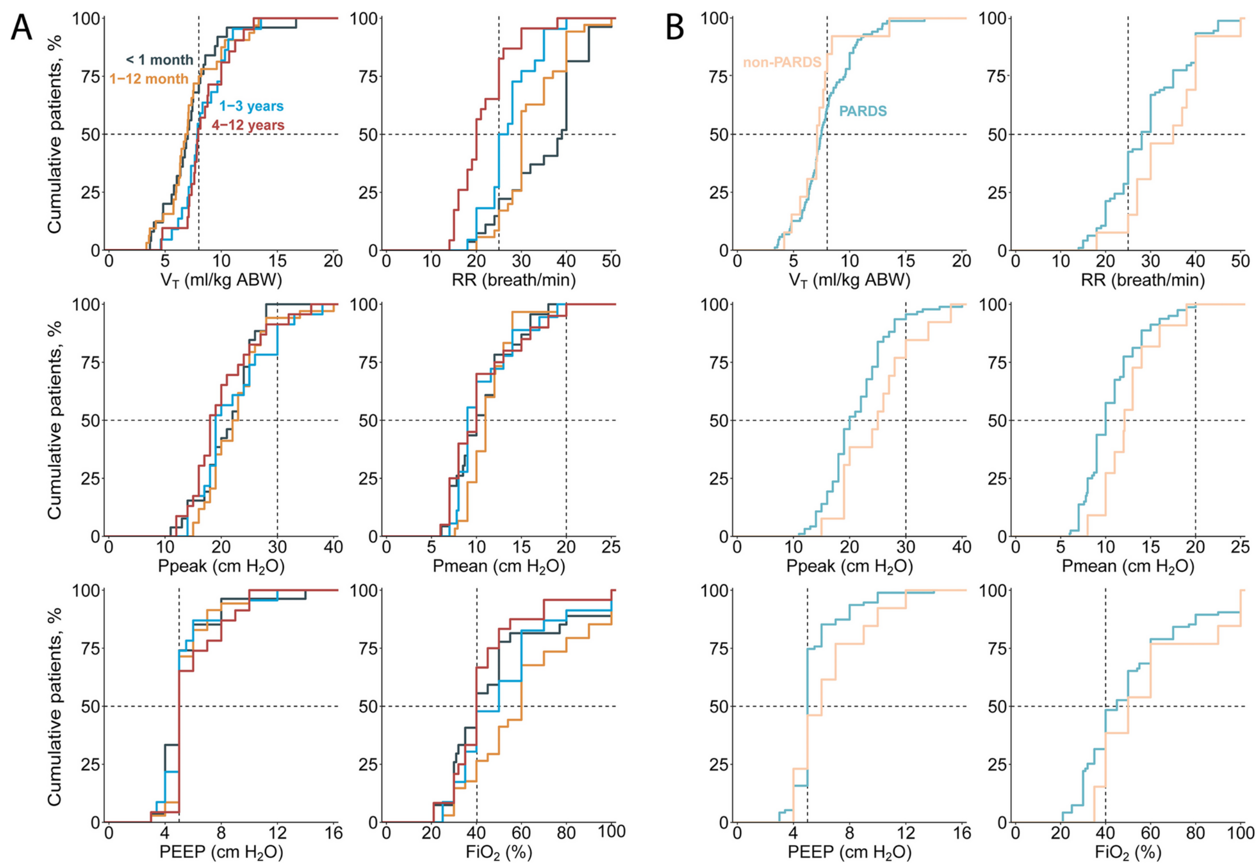

Fig. 3 Cumulative frequency distribution plots of key variables of invasive ventilation at day 0, **A** categorized by age group as well as by **B** the presence or absence of pediatric acute respiratory distress syndrome (PARDS). Horizontal dotted lines represent the median for each variable, and vertical dotted lines represent the ideal cutoff for each parameter. Abbreviations: V_T, tidal volume; PEEP, positive end–expiratory pressure; Pmean, mean airway pressure; Ppeak, peak airway pressure; FiO_2, fraction of inspired oxygen; RR, respiratory rate

number of patients per center may reflect variations in ICU admissions, exclusion of patients expected to need ventilation for < 12 h, and logistical challenges of enrolling within 24 h of initiation. Awareness of data collection could have influenced daily practice. Furthermore, the actual number of patients included was too low to come to firm conclusions. Lastly, these data were collected in 2015/2016, this might hamper generalizability. However, understanding earlier practices remains relevant for evaluating current trends, identifying changes in ventilation management and assessing whether these changes and the introduction of new modalities have improved clinical outcomes of critically ill pediatric patients.

In conclusion, this study gives insight into ventilation practices in critically ill pediatric patients in European centers. Larger studies remain needed to confirm this variability, to investigate associations between ventilation practices and clinical outcomes, and to assess time and geo–economic differences.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s44253-025-00069-2.

Supplementary Material 1

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Authors' contributions
Conceptualization: Martin C.J. Kneyber and Robert G.T. Blokpoel; Methodology: Martin C.J. Kneyber and Robert G.T. Blokpoel; Formal analysis and investigation: Relin van Vliet, David M.P. van Meenen, Frederique Paulus, G. Justin M. Woerlee, and Marcus J. Schultz; Writing—original draft preparation: Relin van Vliet, David M.P. van Meenen, Frederique Paulus and Marcus J. Schultz; Writing—review and editing: Martin C.J. Kneyber, Robert G.T. Blokpoel, Relin van Vliet, David M.P. van Meenen, Frederique Paulus, G. Justin M. Woerlee and Marcus J. Schultz; Funding acquisition: not applicable; Resources: not applicable; Supervision: Martin C.J. Kneyber and Marcus J. Schultz.

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Data availability
A deidentified dataset will be made available upon request to the corresponding author at least 1 year after the publication of this study. The request must include a statistical analysis plan.

Code availability
The R-script is available upon request.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the University Medical Center Groningen, Groningen, the Netherlands (2015/187). Individual patient informed consent was waived because of the strict observational nature of this study.

Consent for publication
Not applicable.

Competing interests
The authors have no relevant financial or non-financial interests to disclose.

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References

1. Gattinoni L, Tonetti T, Cressoni M, Cadringher P, Herrmann P, Moerer O et al (2016) Ventilator-related causes of lung injury: the mechanical power. Intensive Care Med 42(10):1567–1575
2. Heneghan JA, Rogerson C, Goodman DM, Hall M, Kohne JG, Kane JM (2022) Epidemiology of pediatric critical care admissions in 43 United States Children's Hospitals, 2014–2019. Pediatr Crit Care Med 23(7):484–492
3. Farias JA, Frutos F, Esteban A, Flores JC, Retta A, Baltodano A et al (2004) What is the daily practice of mechanical ventilation in pediatric intensive care units? A multicenter study. Intensive Care Med 30(5):918–925
4. Farias JA, Fernández A, Monteverde E, Flores JC, Baltodano A, Menchaca A et al (2012) Mechanical ventilation in pediatric intensive care units during the season for acute lower respiratory infection: a multicenter study. Pediatr Crit Care Med 13(2):158–164
5. Randolph AG, Meert KL, O'Neil ME, Hanson JH, Luckett PM, Arnold JH et al (2003) The feasibility of conducting clinical trials in infants and children with acute respiratory failure. Am J Respir Crit Care Med 167(10):1334–1340
6. Santschi M, Jouvet P, Leclerc F, Gauvin F, Newth CJ, Carroll CL et al (2010) Acute lung injury in children: therapeutic practice and feasibility of international clinical trials. Pediatr Crit Care Med 11(6):681–689
7. Wolfler A, Calderoni E, Ottonello G, Conti G, Baroncini S, Santuz P et al (2011) Daily practice of mechanical ventilation in Italian pediatric intensive care units: a prospective survey. Pediatr Crit Care Med 12(2):141–146
8. Traiber C, Piva JP, Fritsher CC, Garcia PC, Lago PM, Trotta EA et al (2009) Profile and consequences of children requiring prolonged mechanical ventilation in three Brazilian pediatric intensive care units. Pediatr Crit Care Med 10(3):375–380
9. Erickson S, Schibler A, Numa A, Nuthall G, Yung M, Pascoe E et al (2007) Acute lung injury in pediatric intensive care in Australia and New Zealand: a prospective, multicenter, observational study. Pediatr Crit Care Med 8(4):317–323
10. López-Fernández Y, Azagra AM, de la Oliva P, Modesto V, Sánchez JI, Parrilla J et al (2012) pediatric acute lung injury epidemiology and natural history study: Incidence and outcome of the acute respiratory distress syndrome in children. Crit Care Med 40(12):3238–3245
11. Zimmerman JJ, Akhtar SR, Caldwell E, Rubenfeld GD (2009) Incidence and outcomes of pediatric acute lung injury. Pediatrics 124(1):87–95
12. Silva DC, Shibata AR, Farias JA, Troster EJ (2009) How is mechanical ventilation employed in a pediatric intensive care unit in Brazil? Clinics (Sao Paulo) 64(12):1161–1166
13. Tekgüç H, Can FK, Şik G, Demirkol D, Özel D, Yaman A et al (2020) Daily practice of mechanical ventilation and weaning in Turkish PICUs: a multicenter prospective survey. Pediatr Crit Care Med 21(5):e253–e258
14. Newth CJL, Sward KA, Khemani RG, Page K, Meert KL, Carcillo JA et al (2017) Variability in usual care mechanical ventilation for pediatric acute respiratory distress syndrome: time for a decision support protocol? Pediatr Crit Care Med 18(11):e521–e529
15. Albuali WH, Singh RN, Fraser DD, Seabrook JA, Kavanagh BP, Parshuram CS et al (2007) Have changes in ventilation practice improved outcome in children with acute lung injury? Pediatr Crit Care Med 8(4):324–330
16. Kandasamy S, Rameshkumar R, Sangaralingam T, Krishnamoorthy N, Shankar NCG, Vijayakumar V et al (2024) High-flow nasal oxygen in infants and children for early respiratory management of pneumonia-induced acute hypoxemic respiratory failure: the CENTURI randomized clinical trial. Intensive Care Med Paediatr Neonatal 2(1):15
17. Franklin D, Babl FE, George S, Oakley E, Borland ML, Neutze J et al (2023) Effect of early high-flow nasal oxygen vs standard oxygen therapy on length of hospital stay in hospitalized children with acute hypoxemic respiratory failure: the PARIS-2 randomized clinical trial. JAMA 329(3):224–234
18. Schibler A, Pham TM, Dunster KR, Foster K, Barlow A, Gibbons K et al (2011) Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. Intensive Care Med 37(5):847–852
19. Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A (2000) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 342(18):1301–1308
20. Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA et al (2015) Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 372(8):747–755
21. Villar J, Kacmarek RM, Pérez-Méndez L, Aguirre-Jaime A (2006) A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized, controlled trial. Crit Care Med 34(5):1311–1318
22. Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD et al (2010) Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. JAMA 303(9):865–873
23. Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G et al (1998) Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 338(6):347–354
24. Sahetya SK, Mallow C, Sevransky JE, Martin GS, Girard TD, Brower RG et al (2019) Association between hospital mortality and inspiratory airway pressures in mechanically ventilated patients without acute respiratory distress syndrome: a prospective cohort study. Crit Care 23(1):367
25. Schjørring OL, Klitgaard TL, Perner A, Wetterslev J, Lange T, Siegemund M et al (2021) Lower or higher oxygenation targets for acute hypoxemic respiratory failure. N Engl J Med 384(14):1301–1311
26. Costa ELV, Slutsky AS, Brochard LJ, Brower R, Serpa-Neto A, Cavalcanti AB et al (2021) Ventilatory variables and mechanical power in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 204(3):303–311
27. van Meenen DMP, Algera AG, Schuijt MTU, Simonis FD, van der Hoeven SM, Neto AS et al (2023) Effect of mechanical power on mortality in invasively

ventilated ICU patients without the acute respiratory distress syndrome: An analysis of three randomised clinical trials. Eur J Anaesthesiol 40(1):21–28
28. Pisani L, Algera AG, Neto AS, Azevedo L, Pham T, Paulus F et al (2022) Geoeconomic variations in epidemiology, ventilation management, and outcomes in invasively ventilated intensive care unit patients without acute respiratory distress syndrome: a pooled analysis of four observational studies. Lancet Glob Health 10(2):e227–e235
29. Pediatric acute respiratory distress syndrome (2015) consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med 16(5):428–439
30. van Schelven P, Koopman AA, Burgerhof JGM, Markhorst DG, Blokpoel RGT, Kneyber MCJ (2022) Driving pressure is associated with outcome in pediatric acute respiratory failure. Pediatr Crit Care Med 23(3):e136–e144
31. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A et al (2016) Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 Countries. JAMA 315(8):788–800
32. Neto AS, Barbas CSV, Simonis FD, Artigas-Raventós A, Canet J, Determann RM et al (2016) Epidemiological characteristics, practice of ventilation, and clinical outcome in patients at risk of acute respiratory distress syndrome in intensive care units from 16 countries (PRoVENT): an international, multicentre, prospective study. Lancet Respir Med 4(11):882–893
33. Pisani L, Algera AG, SerpaNeto A, Ahsan A, Beane A, Chittawatanarat K et al (2018) PRactice of VENTilation in Middle-Income Countries (PRoVENT-iMIC): rationale and protocol for a prospective international multicentre observational study in intensive care units in Asia. BMJ Open 8(4):e020841
34. Wong JJM, Dang H, Gan CS, Phan PH, Kurosawa H, Aoki K et al (2024) Lung-protective ventilation for pediatric acute respiratory distress syndrome: a nonrandomized controlled trial. Crit Care Med 52(10):1602–1611
35. Botta M, Tsonas AM, Pillay J, Boers LS, Algera AG, Bos LDJ et al (2021) Ventilation management and clinical outcomes in invasively ventilated patients with COVID-19 (PRoVENT-COVID): a national, multicentre, observational cohort study. Lancet Respir Med 9(2):139–148
36. van der Ven F, Blok SG, Azevedo LC, Bellani G, Botta M, Estenssoro E et al (2024) Epidemiology, ventilation management and outcomes of COVID-19 ARDS patients versus patients with ARDS due to pneumonia in the Pre-COVID era. Respir Res 25(1):312
37. Ferrando C, Suarez-Sipmann F, Mellado-Artigas R, Hernández M, Gea A, Arruti E et al (2020) Clinical features, ventilatory management, and outcome of ARDS caused by COVID-19 are similar to other causes of ARDS. Intensive Care Med 46(12):2200–2211
38. Binns E, Koenraads M, Hristeva L, Flamant A, Baier-Grabner S, Loi M et al (2022) Influenza and respiratory syncytial virus during the COVID-19 pandemic: Time for a new paradigm? Pediatr Pulmonol 57(1):38–42
39. Bardsley M, Morbey RA, Hughes HE, Beck CR, Watson CH, Zhao H et al (2023) Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: a retrospective observational study. Lancet Infect Dis 23(1):56–66
40. Izzo F, Comoretto RI, Amigoni A, Daverio M, Zoia E, Diotto V et al (2024) Severe bronchiolitis before and after the COVID-19 pandemic: a retrospective database analysis by the Italian Network of PICU study group (TIPNet). J Anesth Analg Crit Care 4(1):78
41. Guitart C, Bobillo-Perez S, Alejandre C, Armero G, Launes C, Cambra FJ et al (2022) Bronchiolitis, epidemiological changes during the SARS-CoV-2 pandemic. BMC Infect Dis 22(1):84
42. Brisca G, Mariani M, Buratti S, Ferretti M, Pirlo D, Buffoni I et al (2023) How has the SARS-CoV-2 pandemic changed the epidemiology and management of acute bronchiolitis? Pediatr Pulmonol 58(4):1169–1177
43. Bhalla AK, Klein MJ, Emeriaud G, Lopez-Fernandez YM, Napolitano N, Fernandez A et al (2021) Adherence to lung-protective ventilation principles in pediatric acute respiratory distress syndrome: a pediatric acute respiratory distress syndrome incidence and epidemiology study. Crit Care Med 49(10):1779–1789
44. Lee JH, Rehder KJ, Williford L, Cheifetz IM, Turner DA (2013) Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature. Intensive Care Med 39(2):247–257
45. Milani GP, Plebani AM, Arturi E, Brusa D, Esposito S, Dell'Era L et al (2016) Using a high-flow nasal cannula provided superior results to low-flow oxygen delivery in moderate to severe bronchiolitis. Acta Paediatr 105(8):e368–e372
46. Wing R, James C, Maranda LS, Armsby CC (2012) Use of high-flow nasal cannula support in the emergency department reduces the need for intubation in pediatric acute respiratory insufficiency. Pediatr Emerg Care 28(11):1117–1123
47. Ramnarayan P, Richards-Belle A, Drikite L, Saull M, Orzechowska I, Darnell R et al (2022) Effect of high-flow nasal cannula therapy vs continuous positive airway pressure therapy on liberation from respiratory support in acutely Ill children admitted to pediatric critical care units: a randomized clinical trial. JAMA 328(2):162–172
48. Ramnarayan P, Richards-Belle A, Drikite L, Saull M, Orzechowska I, Darnell R et al (2022) Effect of high-flow nasal cannula therapy vs continuous positive airway pressure following extubation on liberation from respiratory support in critically Ill children: a randomized clinical trial. JAMA 327(16):1555–1565
49. Krasinkiewicz JM, Friedman ML, Slaven JE, Tori AJ, Lutfi R, Abu-Sultaneh S (2020) Progression of respiratory support following pediatric extubation. Pediatr Crit Care Med 21(12):e1069–e1075
50. Khemani RG, Smith L, Lopez-Fernandez YM, Kwok J, Morzov R, Klein MJ et al (2019) Paediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE): an international, observational study. Lancet Respir Med 7(2):115–128
51. Schouten LR, Veltkamp F, Bos AP, van Woensel JB, SerpaNeto A, Schultz MJ et al (2016) Incidence and mortality of acute respiratory distress syndrome in children: a systematic review and meta-analysis. Crit Care Med 44(4):819–829
52. Flori HR, Glidden DV, Rutherford GW, Matthay MA (2005) Pediatric acute lung injury: prospective evaluation of risk factors associated with mortality. Am J Respir Crit Care Med 171(9):995–1001

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