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Premature Infants Show Consistently Good Lung Compliance During Conventional Mechanical Ventilation

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ABSTRACT

Introduction: Many extremely small preterm infants need to be intubated and mechanically ventilated during their intensive care stay. Animal studies indicate that lung compliance can deteriorate rapidly under conventional ventilation. This study investigated whether this presumed deterioration in compliance actually occurs in extremely small preterm infants.

Methods: Data from 56 conventionally ventilated preterm infants born from 2016 to 2022 at 25.22 weeks' gestation (±1.47) and 678.71 g (±138.14) birth weight were retrospectively analysed. This study investigated how dynamic compliance changed over the course of ventilation.

Results: The infants were conventionally ventilated from 7.25 days of life (±5.59) for 2.68 days (±2.35). Compliance at the beginning was 0.37 mL/cmH_2O/kg (±0.17), after 1 h 0.38 mL/cmH_2O/kg (±0.16), after 3 h 0.40 mL/cmH_2O/kg (±0.20), after 6 h 0.44 mL/cmH_2O/kg (±0.23), after 24 h 0.46 mL/cmH_2O/kg (±0.17) and after 48 h 0.43 mL/cmH_2O/kg (±0.13). The increase in compliance compared to baseline was statistically significant after 12 ($p = 0.016$) and 24 h ($p = 0.042$). Ventilation was performed with a PEEP of 7.51 cmH_2O (±1.16) and a peak pressure of 20.64 cmH_2O (±2.73). All received surfactant after birth and 21 (37.5%) also at the start of conventional ventilation.

Conclusion: During conventional ventilation in premature infants after administration of surfactant and with basically recruited lungs, no deterioration in compliance was observed either in the short or long term. The PEEP of almost 7.5 cmH_2O used may have contributed to the fact that the deterioration described in the animal model did not occur in the preterm infants.

1 | Introduction

The current guidelines recommend the administration of surfactant in preterm infants according to LISA protocol [1]. LISA defines the administration of surfactant via a thin catheter while the preterm infant is breathing spontaneously on CPAP [2]. Both surfactant and CPAP synergistically improve and stabilise lung compliance [3, 4]. Nevertheless, 40%–70% of premature babies have to be intubated and ventilated during their intensive care stay [2, 5–7]. Animal studies in rats, rabbits and lambs show that compliance in premature or surfactant-depleted animals under conventional ventilation decreases dramatically within a few hours [8–10]. These studies have led to the assumption that human preterm infants would also show a dramatic deterioration in lung compliance during conventional ventilation. This is one of the reasons why conventional ventilation in small preterm infants is considered inferior to high-frequency ventilation in terms of lung-protective ventilation.

Compliance describes the distensibility of the lungs, that is, the volume that can flow into the lungs at a certain pressure change. At low pressures and low volumes, compliance is physiologically low, as the alveoli must be opened first and more pressure is required for this [11]. The same applies to compliance at high pressures and high volumes, as the lungs are already maximally filled. The focus of this study is on dynamic compliance, which is determined during normal breathing and is influenced by flow resistance [12].

The aim of the study is to find out whether the deterioration in compliance shown in the animal model can also be demonstrated in conventionally ventilated extremely preterm infants and, if so, to what extent and after how long.

2 | Materials and Methods

This study is a retrospective single-centre study conducted at Salzburg University Hospital. Due to the retrospective data analysis, no informed consent was required.

Patients were recruited according to the following criteria.

2.1 | Inclusion Criteria

- Date of birth from 2016 to 2022.
- Pregnancy duration of less than 28 + 0 weeks gestation.
- Birth weight of less than 1000 g.
- Continuous conventional ventilation in the first 21 days of life for more than 24 h until extubation.

2.2 | Exclusion Criteria

- Postnatal transfer after birth outside the centre.
- Death in the delivery room or intensive care unit.
- Start conventional ventilation in the delivery room before the first surfactant is administered.
- Chromosomal or relevant genetic disorders.
- Hemodynamically relevant cardiac malformations.
- Congenital lung malformations.

All preterm infants who received continuous conventional ventilation in the first 21 days of life were included in the study. Neither the reason for intubation nor whether or not the infants were on high-frequency ventilation before this conventional ventilation phase was taken into account. Only transferred infants, infants who died on the ward and infants with relevant congenital malformations were excluded. Premature babies who were transferred to the centre have different characteristics than babies born in the centre. They were therefore excluded, as were premature babies with malformations relevant to ventilation. Children who died on the ward were excluded because their ventilation settings were often neither checked nor corrected over a longer period of time.

In Salzburg, premature babies are generally given spontaneous breathing and if they are born before 28 + 0 weeks of gestation, they are routinely administered surfactant via a thin catheter. Surfactant is also administered generously to these children if they have to be intubated and ventilated during the first few days, as well as mixed with budesonide during weaning. Ventilation is performed with Sophie 2020 (Fritz Stephan GmbH, Gackenbach, Germany) and it is not uncommon to recruit the lungs of premature babies after intubation using high-frequency ventilation.

The main target parameter was compliance (C) during the course of the first documented conventional ventilation. To calculate compliance, the ventilation data expiratory tidal volume (Vte), peak inspiratory pressure (PIP) and positive end-expiratory pressure (PEEP), which were electronically recorded every minute, were extracted from the electronic patient database (MetaVision, Version 5.46.42, iMDsoft, Tel Aviv, Israel). To describe the demographic data of the group, birth weight, gestational age and gender as well as weight at the beginning and end of ventilation were recorded. To describe the clinical condition, oxygen demand (FiO_2) and mean airway pressure (MAP) were recorded in the 32 h before the start of conventional ventilation. The respiratory severity score (RSS) was calculated as the product of $FiO_2 \times MAP$ [13]. Clinical data such as prenatal steroids, administration of surfactant immediately before or after the start of conventional ventilation and recruitment with high-frequency ventilation were also recorded.

Compliance was calculated using the formula $C = Vte/(PIP - PEEP)$, whereby the values were documented every minute. To establish a relationship with weight, this was extrapolated linearly from the weight at the start of ventilation to the weight at the end of ventilation for each day.

To be able to assess the effects of the ventilation strategies, mortality and morbidity data for the years of birth studied were collected as additional secondary outcome measures from the Vermont Oxford Network (VON). In accordance with the classification of the Vermont Oxford Network, all preterm infants born between 22- and 29-weeks' gestation in Salzburg between 2016 and 2022 were examined. The parameters examined were survival, survival without morbidity, oxygen requirement at week 36 of hospitalisation and chronic lung disease. The results of the individual years were summarised and compared with the summarised results of the European group of the Vermont–Oxford network.

Statistics: As the PIP and Vte values are strongly dependent on the spontaneous breathing of the child, a moving average over an interval of 10 min was calculated for these variables in the same way as for the PEEP values. A window of 5 min was defined for the baseline values. These values were used to calculate dynamic compliance over time. To determine the changes in compliance over time, the difference from baseline was analysed at nine time points: 1, 3, 6, 9, 12, 24, 48, 96 and 120 h after the start of ventilation. Means, standard deviations and absolute and relative frequencies were calculated to describe the characteristics, explanatory and outcome variables. In addition, the Wilcoxon signed rank test was used to analyse whether there were differences in the change in compliance between the initial timepoint and following individual time points. The Pearson correlation coefficient was used to analyse the correlations between the change and metric variables (e.g., week of birth). Line graphs and boxplots were used for visualisation, where, if necessary, a logarithmic transformation of the data was used to better visualise the differences.

A two-sided significance level of 5% was used for all hypothesis tests and for multiplicity was corrected using Bonferroni-Holm.

The results of all analyses were calculated using the statistical software package R (Version 4.3.2).

The conduct of the study was approved by the responsible ethics committee of Salzburg on 06.04.2023 with the number 1035/2023.

3 | Results

From 2016 to 2022, 146 premature babies born before 28 + 0 weeks of gestation and with a birth weight of < 1000 g were cared for in Salzburg. Of these, five premature babies were transferred to the centre from outside, 24 died, 50 were not ventilated at all and 11 were not ventilated conventionally within 21 days. After excluding these children, 56 premature babies could be included in the study. Figure 1 shows the flow chart for patient recruitment, further demographic and clinical data can be found in Table 1.

Of the 56 premature babies included, 29 (51.79%) were female and 27 (48.21%) male. The average gestational age was 25.22 weeks' gestation (±1.47). The average birth weight was 678.71 g (±138.14). All preterm infants included in the study were administered a less invasive surfactant administration (LISA) after birth. A further 21 (37.5%) preterm infants were administered surfactant at the start of conventional ventilation.

The average time between birth and the start of invasive conventional ventilation was 7.25 days (±5.59). The respiratory severity score (RSS) 32 h before intubation was 3.52 (±1.69; p-value 0.004), 16 h before intubation 3.67 (±2.09; p-value 0.002), 8 h before 3.94 (±2.19; p-value 0.002), 4 h before 4.29 (±2.40; p-value 0.186), 2 h before 4.42 (±2.26; p-value 0.186), 1 h before 4.89 (±3.01) and immediately before intubation 4.12 (±3.11; p-value 0.007). The p-values refer to the maximum value 1 h before start of or switch to conventionally ventilation. The courses of FiO_2, MAP and RSS are shown graphically in Figure 2. The premature babies were conventionally ventilated for an average of 2.68 days (±2.35).

TABLE 1 | Presentation of the demographic and anthropometric data of the preterm infants included in the study.

***n* = 56**	**Mean**	**SD**
Gestational week	25.22	1.47
Birth weight (g)	678.71	138.14
Birth length (cm)	31.18	2.14
Head circumference (cm)	22.64	1.71
Weight begin conventional ventilation (g)	765.66	217.93
Weight end conventional ventilation (g)	886.11	237.95
Start of conventional ventilation (d)	7.25	5.59
Duration of conventional ventilation (d)	2.69	2.35
Sex *n* (%)	f: 29 (51.71)	m: 27 (48.21)

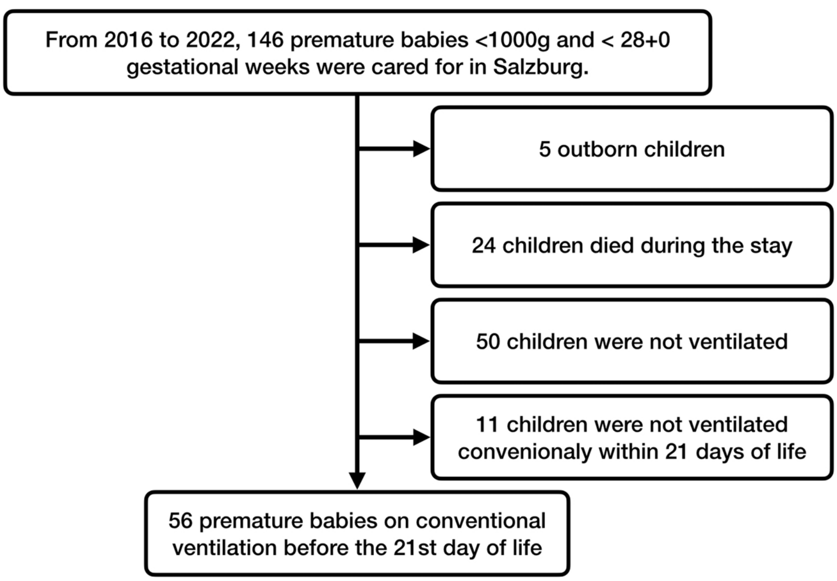

FIGURE 1 | Flow chart of all patients screened for the study.

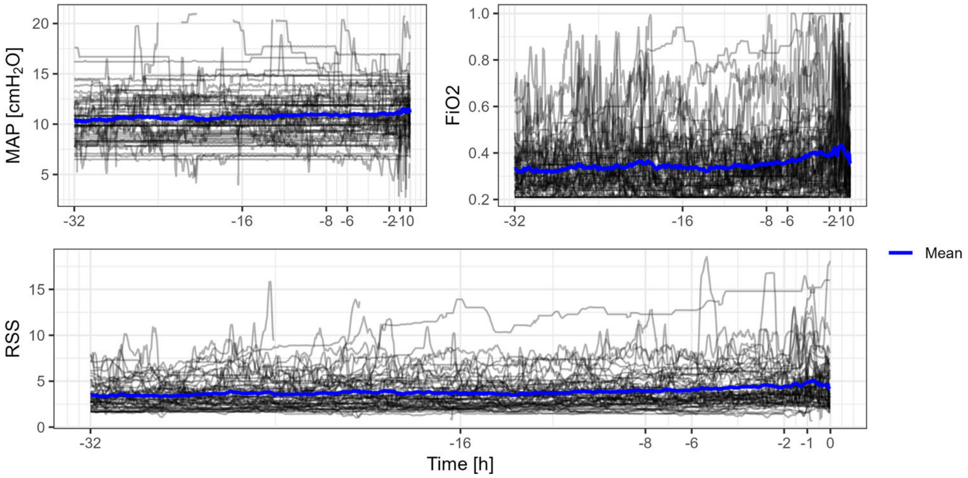

FIGURE 2 | Graph of positive end-expiratory pressure (PEEP), oxygenation (FiO_2) and respiratory severity score (RSS) in the 8 h before intubation. The individual courses of the infants are shown in grey and the mean values as a thick blue line.

Compliance at the beginning was 0.28 mL/cmH_2O (±0.26), after 1 h 0.28 mL/cmH_2O (±0.29), after 3 h 0.30 mL/cmH_2O (±0.29), after 6 h 0.34 mL/cmH_2O (±0.30), after 12 h 0.38 mL/cmH_2O (±0.32), after 24 h 0.37 mL/cmH_2O (±0.33), after 48 h 0.36 mL/cmH_2O (±0.31) after 72 h 0.45 mL/cmH_2O (±0.43) after 96 h 0.47 mL/cm H_2O (±0.41) and after 120 h 0.43 mL/cmH_2O (±0.38).

The measured values of PEEP, PIP and Vte as well as Vte and compliance in relation to body weight and the difference in compliance at the measurement times compared to the baseline value are listed in Table 2. Ventilation was performed with a PEEP of 7.51 cmH_2O (±1.16) and a peak pressure of 20.64 cmH_2O (±2.73). Figure 3 shows the individual progression of PEEP, PIP, Vte and compliance over the course of the ventilation time. The deviation of compliance from the initial value of all patients together as well as divided into the groups with and without surfactant administration at the start of conventional ventilation is shown in Figure 4 on a logarithmic scale. At no time was there a statistically significant difference between the children with and without surfactant.

In Salzburg, a total of 89.86% (±2.69) of all premature babies with a gestational age of 22 to 29 weeks survived from 2016 to 2022. The survival rate without morbidities was 53.64% (±6.12). 13.48% (±8.85) of preterm infants required oxygen at 36 weeks gestation and 11.79% (±8.44) were diagnosed with BPD. A comparison with the European group of the Vermont Oxford Network including odds ratio is listed in Table 3.

4 | Discussion

The data collected show that there is no decrease in compliance under mechanical ventilation of extremely preterm infants even after 120 h. There was also no initial deterioration in the first hours of conventionally ventilation. On the contrary, the data show that compliance actually increases over the course of conventional mechanical ventilation in the preterm infants we ventilate. The improvement compared to the initial value is statistically significant from the sixth hour of ventilation. Animal studies have shown that compliance can decrease dramatically within a few hours under conventional ventilation in animal models [8–10]. In the studies by McMulloch et al. and Muscedere et al. adult animals were ventilated with NaCl 0.9% after bronchopulmonary lavage. Both showed a dramatic decrease in compliance under conventional ventilation [8, 10]. However, McMulloch et al. were able to show that the animals under high-frequency ventilation showed a significantly better course of compliance, especially when regular recruitment manoeuvres were performed. Exactly this compliance behaviour was also shown in the study by Miedema et al. [9]. However, this study was conducted on premature lambs after primary surfactant deficiency, whose lungs can be compared very well with those of premature infants. This may well have led to the conclusion that compliance would also drop as quickly in conventionally ventilated premature infants as was shown in the animal studies.

The data now available were collected from premature infants who did not have to be intubated immediately after birth due to surfactant deficiency. All of these infants showed a secondary deterioration after initially adequate surfactant replacement. All of these preterm infants received surfactant according to the LISA protocol recommended for preterm infants [1]. Surfactant and CPAP, both integral components of LISA protocol, have a synergistic effect on lung compliance [3, 4]. Despite this initial surfactant administration and a high administered MAP, the respiratory function of the premature infants increasingly deteriorated, as documented by the RSS on the day before conventionally ventilation. During this phase, some of the children also received surfactant again. This, as well as lung recruitment, certainly had a positive effect on the lung compliance of these children [14]. However, the influence of the surfactant was not statistically detectable.

Nonetheless, compliance with conventional ventilation did not deteriorate in these children, but actually improved. The premature infants included in this study were ventilated with an average PEEP of 8 cmH_2O, an average PiP of 20 cmH_2O and an average Vte of just under 5 mL/kg. It is striking that the Vte used of 4 ml/kg tends to be in the low range and the PEEP of 8 cmH_2O tends to be in the higher range of the usual

TABLE 2 | Measured values and calculated values of all data collected at the measurement times.

$n = 56$	PEEP (cmH_2O)			PIP (cmH_2O)			Vte (mL)			Vte (mL/kg)			C (mL/cmH_2O/kg)			Compliance change (mL/cmH_2O/kg)			
Time	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	*p*-value
0	7.88	1.32	8.00	22.73	5.09	22.00	3.89	1.84	3.48	5.16	2.02	5.31	0.374	0.166	0.374	—	—	—	—
1	7.74	1.31	7.94	22.25	4.76	21.05	3.87	1.69	3.74	5.18	1.99	5.19	0.377	0.156	0.371	0.0033	0.1316	0.0077	0.8575
3	7.53	1.37	7.41	21.83	4.94	21.10	3.90	1.67	3.80	5.28	2.08	4.96	0.402	0.200	0.361	0.0227	0.1709	0.0046	0.8575
6	7.35	1.30	7.11	20.85	4.49	20.00	4.18	2.16	3.72	5.52	2.25	5.22	0.437	0.229	0.406	0.0625	0.1736	0.0345	0.0844
12	7.36	1.32	7.05	20.73	3.64	20.00	4.74	2.86	4.21	6.20	2.82	5.55	0.475	0.256	0.391	0.1030	0.2330	0.0561	0.0425
24	7.48	1.27	7.24	20.57	3.68	20.00	4.71	2.44	3.89	6.31	2.58	5.85	0.458	0.171	0.423	0.0886	0.1882	0.0812	0.0162
48	7.56	1.07	7.94	21.10	3.53	21.50	4.70	1.91	4.28	6.28	1.49	6.16	0.428	0.127	0.402	0.0445	0.2076	0.0246	0.6253
72	7.77	1.06	7.95	21.14	3.87	21.00	5.85	2.95	5.45	7.53	2.88	6.33	0.505	0.220	0.476	0.1132	0.2472	0.1510	0.2623
96	7.74	0.85	8.00	20.04	2.14	19.95	5.45	2.76	4.84	6.93	1.79	6.54	0.481	0.172	0.446	0.1111	0.2104	0.1271	0.3235
120	8.08	1.56	8.15	21.39	2.56	22.00	5.17	2.51	4.61	7.06	1.82	7.45	0.459	0.225	0.426	0.0438	0.2716	0.0650	0.8575

Abbreviations: C, compliance; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; SD, standard deviation; Vte, expiratory tidal volume.

recommendations for ventilating preterm infants [7, 15, 16]. The data situation for preterm infants with regard to the optimal PEEP is rather weak, there are hardly any studies on different PEEP values, PEEP is described in the literature as a very 'individual' parameter [15–17]. However, PEEP is described as a key component of lung-protective mechanical ventilation [18]. The lower inflation point (LIP) of the pressure-volume curve should be taken into account to set the PEEP in a way that is gentle on the lungs. At the beginning of the pressure-volume curve, at low pressures and small lung volumes, the alveoli are still closed and must first be opened. The Young–Laplace equation describes that more pressure must be applied to open small alveoli than to keep open alveoli that are already open. Consequently, more pressure is required at the lower part of the curve to open the lungs and compliance is low [11]. If a lung is ventilated in the lowest part of its expansion curve, it must be assumed that large sections of the lung are atelectatic, that is, collapsed. In these poorly ventilated lungs, atelectatic alveoli are located next to open areas. The tidal volume administered via ventilation can therefore not be distributed evenly over the entire alveolar volume. Atelectatic areas hardly open at all, so that the already open areas have to absorb the entire tidal volume. The consequences can be structural damage and overinflation. The LIP marks the pressure at which most of the collapsed alveoli can be opened [19]. This is where the surfactant comes into play. By reducing the surface tension, the pressure required to open the alveoli is lowered in accordance with Laplace's law. This drastically improves lung compliance [20]. To ensure that as many alveoli as possible remain open during conventional ventilation, it is postulated that the PEEP should be higher than the LIP [21]. The study by Muscedere et al. clearly shows why this should be the case. In this study, adult rats were ventilated after NaCl lavage. Animals with a PEEP < LIP (0 and 4 cmH_2O) showed a loss of compliance after a few hours of ventilation, whereas with a PEEP > LIP (15 cmH_2O) compliance remained good over the course of ventilation [10]. Similar observations were made by McMulloch et al. In this study, adult rabbits were also ventilated after lavage either conventionally with a PEEP of 8 cmH_2O or by means of high-frequency ventilation plus recruitment manoeuvres. The conventionally ventilated animals showed a loss of compliance, the animals recruited to high-frequency ventilation did not, the non-recruited animals to high-frequency ventilation were in between [8]. In adult animals after bronchopulmonary lavage with NaCl, a PEEP of 8 cmH_2O on conventional ventilation thus appears to be significantly < LIP, which is why the alveoli collapse in accordance with Young–Laplace's law. In premature infants, the LIP is between 10 and 15 cmH_2O [9, 22]. A PEEP of 5 cmH_2O or less is therefore always considerably below the LIP. However, even a PEEP of 8 cmH_2O is theoretically still below the average LIP of premature infants, but it is closer to it. Also, unlike in the studies described above, a fixed PEEP of 8 cmH_2O was not set, but the 7.5 mmH_2O was the mean value. The dispersion over time is shown in Figure 3. The PEEP was set according to the clinic and thus the compliance of the lungs without a fixed specification. In principle, this allows more alveoli to be kept open more effectively, which can result in more efficient ventilation.

The Young–Laplace equation describes why open lung sections can be kept open with lower pressures than previously used to

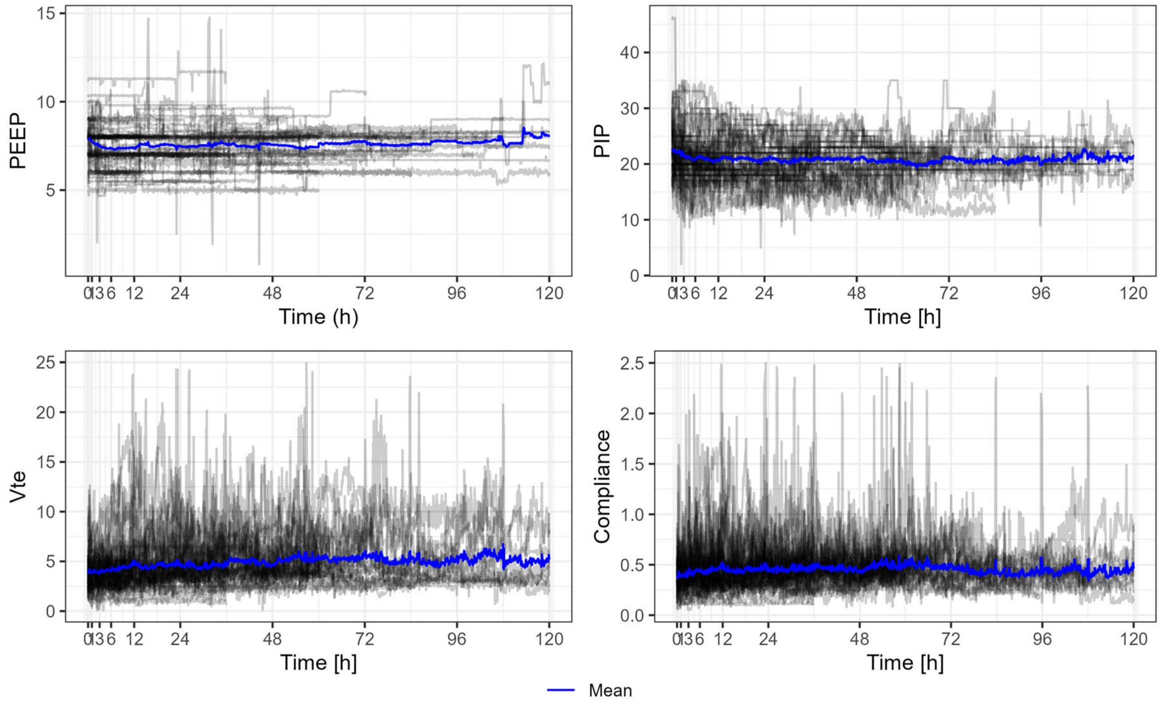

FIGURE 3 | Graphical representation of positive end-expiratory pressure (PEEP; cmH_2O), peak inspiratory pressure (PIP; cmH_2O), expiratory tidal volume (Vte; mL) and compliance compared to bodyweight ($mL/cmH_2O/kg$). The individual courses of the infants are shown in grey and the mean values as a thick blue line.

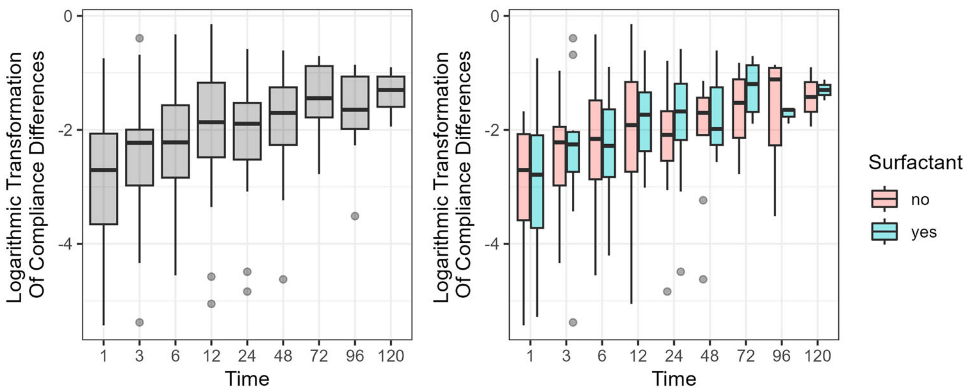

FIGURE 4 | Representation of the deviation of compliance from the initial value of all patients together as well as divided into the groups with and without surfactant administration at the start of conventional ventilation is shown on a logarithmic scale.

TABLE 3 | Comparison of the outcome figures of all premature infants with a gestational age of 22 to 29 weeks from 2016 to 2022 from Salzburg with the European group of the Vermont Oxford Network (VON-EG).

	OR	Salzburg % (SD)	VON-EG % (SD)
Survival	1,984	89.86 (2.69)	81.39 (0.73)
Survival without morbidities	1,453	53.64 (6.12)	44.2 (0.71)
Oxygen—at 36 weeks	0,267	13.48 (8.85)	37.24 (1.38)
Chronic lung disease	0,299	11.79 (8.44)	30.77 (1.18)

Abbreviations: OR, odds ratio; SD, standard deviation.

open atelectatic alveoli. This results in the typical hysteresis curve of lung compliance. During conventional ventilation, alveoli are opened and thus recruited with each breath. Subsequently, lower pressures are required to keep the opened lung sections open. This function is performed by PEEP. The PEEP used, together with the PIP, is responsible for the MAP (mean airway pressure) [23–25]. A generally higher PEEP setting during conventional ventilation therefore results in a higher

MAP, which in turn contributes to a larger gas exchange surface. This reduces the volume difference between open and atelectatic areas so that the tidal volume can be better distributed over the entire lung and counteract overinflation of individual sections. Overall, it is therefore not surprising that a correctly selected PEEP is a key component of lung-protective mechanical ventilation [18]. This consideration speaks against fixed PEEP values and in favour of adapting the PEEP to the respective situation of the lungs to be ventilated. We therefore believe that a PEEP that is dynamically adapted to the situation and correspondingly high can prevent a deterioration in compliance due to conventional ventilation in premature babies.

Ultimately, however, it can also be assumed that the improvement in compliance over the course of ventilation is not only due to lung mechanical causes, but also to a significant extent to weaning from ventilation. If the children are ventilated using Volume Target Ventilation, the machine automatically reduces the peak pressure [26]. This reduces the driving pressure, which automatically improves compliance while the tidal volume remains the same. Overall, however, this is definitely a sign of a clinical improvement in the situation.

Every mechanical ventilation has an effect on many organ systems in premature infants, primarily on the lungs, of course. Despite all the advances in neonatology, bronchopulmonary dysplasia remains a relevant factor in the morbidity of former premature infants, which continues to correlate with ventilation [5]. However, other complications also play a role in assessing the outcome of small preterm infants. Many of these correlates with ventilation and BPD [27]. Particularly relevant for morbidity are high-grade cerebral haemorrhages or other complications such as necrotising enterocolitis or retinopathy of prematurity [28]. The data collected show that the small preterm infants cared for in Salzburg in the years studied generally had a very high survival rate without any morbidity and, above all, a very low BPD rate compared to the Vermont Oxford Network.

One limitation of the study is that the available data do not guarantee that there is complete pressure equalisation into the alveolus at the end of inspiration. It can be assumed that there is regularly still a certain flow in the airways. This is due to the high resistance of the small airways in small preterm infants and cannot be proven with the data collected. The measured values can therefore correspond to dynamic compliance and not static compliance [12]. Dynamic compliance is influenced by both elastic resistance and flow resistance in the lungs. Static compliance is therefore always higher, that is, better than dynamic compliance. Leakage from the tube also reduces the measured compliance [29]. The ventilation pressure must overcome the tube leak to reach the tidal volume. Leakage data were not collected in this study but are always to be expected in premature infants. It can therefore be assumed that the static compliance of children is actually somewhat higher than the compliance actually measured. The true values may therefore lie within the range of values described in the literature [12, 29]. As the data was collected retrospectively, other external confounding factors cannot be filtered out with certainty. As is well known, every retrospective study as such harbours the risk of information bias. In addition, the lack of compliance data during high-frequency ventilation limits the conclusions of this study. Further prospective studies based on these retrospective data and in comparison, with children on high-frequency ventilation are therefore desirable.

Another limitation of the study is the patient selection based on the inclusion and exclusion criteria and the fact that it is a retrospective study. All conventionally ventilated preterm infants were included, with the exception of died and transferred preterm infants. This means that the data includes preterm infants with very different lung situations. The main similarity in all premature babies is that conventional ventilation was not primarily started in the delivery room but always secondarily on the ward. Irrespective of this, however, selection cannot be ruled out. In addition, automatically recorded data was used for the study. The ventilator supplies data to the electronic patient database every second. A single value is documented there every minute without selection or filtering. The stored data does not necessarily have to represent the unsaved data in between. As it is known that both pressure and volume data react very sensitively to, for example, condensation or restlessness of the patient, a certain falsification of the data is unavoidable. An attempt was made to compensate for this by using a moving average over a 10-min interval. In addition, four patients were excluded due to unusable data.

5 | Conclusion

Secondary conventional ventilation in preterm infants with initially well-recruited lungs is not a risk factor for a deterioration in compliance, regardless of how recruitment was performed at the start of ventilation. One possible reason for the observed improvement in compliance may be the higher PEEP setting. A higher PEEP closer to the lower opening pressure of the lungs can both keep the alveoli open more effectively and reduce the proportion of atelectatic areas via the higher MAP. Consequently, the tidal volume can be distributed more evenly and the pressure gradients between open and closed alveoli can be reduced. The gas-exchanging surface can thus be increased, and ventilation can be both efficient and protective.

Author Contributions

Annalena Reiss: data curation, formal analysis, writing–original draft. **Wanda Lauth:** writing–review and editing, formal analysis, visualisation. **Martin Wald:** conceptualisation, methodology, supervision, writing–review and editing, resources.

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Ethics Statement

The conduct of the study was approved by the responsible ethics committee of Salzburg on 06.04.2023 with the number 1035/2023.

Conflicts of Interest

Martin Wald has been a consultant for the companies Fritz Stephan GmbH and medin Medical Innovations GmbH and has given paid lectures for Medtronic Österreich GmbH during the past 3 years. He has also organised workshops sponsored by the above companies. All other authors have no conflicts of interest to declare.

Data Availability Statement

The raw data from the in vitro simulations are available from the corresponding author upon reasonable request.

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