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Respiration and the Airway

RESPIRATION AND THE AIRWAY

Evaluation of the intratidal compliance profile at different PEEP levels in children with healthy lungs: a prospective, crossover study

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Abstract

Background: Optimal intraoperative lung protective ventilation (LPV) strategies in young children are largely underexplored. Individualised PEEP levels are likely to contribute to optimal lung protection. We determined optimal PEEP levels in young children during general anaesthesia by evaluating changes in intratidal compliance with varying PEEP.

Methods: Children aged ≤6 yr were enrolled in this prospective interventional study. After induction of general anaesthesia and neuromuscular block (rocuronium), children were randomly assigned to be mechanically ventilated at each of three PEEP levels for 15 min each: 5, 8, and 12 cm H_2O PEEP ($PEEP_{5/8/12}$). Haemodynamic and respiratory data were recorded at each PEEP level. Intratidal volume-compliance was classified into one of six compliance profiles (increasing/decreasing/horizontal [plateau]/increasing-horizontal/horizontal-decreasing/increasing-horizontal-decreasing) at each PEEP level. The primary outcome was intratidal compliance at different PEEP levels.

Results: Forty-seven children were enrolled (40% female; median age: 2.5 yr [0.9–3.7]). Mean airway pressure progressively increased from 7.6 cm H_2O (0.5) at $PEEP_5$, 10.5 cm H_2O (0.9) at $PEEP_8$ to 14.3 cm H_2O (0.5) $PEEP_{12}$ ($P<0.001$). Mean driving pressure was lower at $PEEP_{12}$ (6.3 cm H_2O [1.1]), compared with $PEEP_8$ (6.5 cm H_2O [1.1]) and $PEEP_5$ (7.0 cm H_2O [1.5]; $P=0.004$ for trend). Intratidal compliance increased in 31/47 (66%) children at $PEEP_5$, but was less likely with $PEEP_8$ (9/47; 19.1%) and was absent at $PEEP_{12}$. At $PEEP_8$, plateaued compliance was most frequent (16/46; 34.8%). At $PEEP_{12}$, decreasing compliance occurred most frequently (32/46; 69.6%).

Conclusions: Intratidal compliance at different PEEP levels varied widely in young children under general anaesthesia. These data suggest that individualised PEEP levels are required for optimal lung protection in children.

Clinical trial registration: NCT03533296.

Keywords: general anaesthesia; lung compliance; lung protection; mechanical ventilation; paediatrics; PEEP

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Editor's key points

- Optimal intraoperative lung protective strategies in young children are unknown.
- Individualised PEEP levels are likely to contribute to optimal lung protection.
- The authors are the first to measure intratidal compliance in children (aged 1–6 yr) in order to determine optimal PEEP during general anaesthesia.
- Optimal PEEP defined as intratidal compliance profiles consistent with less derecruitment and/or overdistension ranged from 5 to 12 cm H_2O.
- These data suggest that individualised PEEP levels are required for optimal lung protection in children.

Prevention of ventilator-induced lung injury reduces the mortality and morbidity in patients undergoing mechanical ventilation in the intensive care unit or operating room.[1–3] Lung-protective ventilation (LPV) strategies, including low tidal volume (V_T), PEEP, and lung recruitment manoeuvres,[4] reduce mortality in patients with acute respiratory distress syndrome (ARDS)[1,5] and improve operative outcomes.[3,6] However, data regarding intraoperative LPV in children are limited; there has been only one randomised controlled trial for this population.[7]

Children are more vulnerable to atelectasis than adults[8] having different chest wall characteristics as compared with those of adults.[9] PEEP >6 cm H_2O improved the Pa_{O_2} in children with ARDS.[10] However, there have been limited studies to determine the appropriate PEEP level in paediatric patients undergoing general anaesthesia for surgery. Wirth and colleagues[11] found that a PEEP of 5 cm H_2O resulted in more homogeneous regional ventilation, in comparison with PEEP set at 2 cm H_2O; however, intratidal recruitment/derecruitment was not prevented.

To ensure an appropriate PEEP that avoids both atelectasis and overdistension, individualising PEEP settings appears to be optimal.[12–15] Individualised PEEP levels can be accomplished by minimising the driving pressure,[13] measuring the transpulmonary pressure using an oesophageal manometer,[15] and utilising thoracic impedance tomography.[14] Intratidal compliance-volume profile analysis using the gliding-SLICE method[14,16,17] enables assessment of alveolar recruitment/derecruitment or overdistension during tidal ventilation. A horizontal (plateau) compliance profile indicates the absence of recruitment/derecruitment or overdistension, whereas increasing or decreasing compliance profiles indicate recruitment/derecruitment or overdistension in intratidal volume ventilation, respectively.[14,16] The usefulness of intratidal compliance assessment has been demonstrated in adults with ARDS[18] and those undergoing surgery[14,16] but has never been explored in young children.

We hypothesised that the intratidal compliance-volume profile differs according to PEEP and that appropriate PEEP during general anaesthesia in mechanically ventilated young children with healthy lungs would be more than 5 cm H_2O. To determine the appropriate PEEP, we evaluated the intratidal compliance profile distribution at different PEEP levels in children with normal lungs during general anaesthesia.

Methods

Ethics and study population

We conducted a single-centre, prospective interventional study performed in a tertiary children's hospital.

The study was approved by the Institutional Review Board of Seoul National University Hospital (H1804-101-938; date of approval: May 23, 2018) and registered at http://clinicaltrials.gov/ (number: NCT03533296; principal investigator: KJT; date of registration: May 11, 2018). The study was performed according to the ethical standards set by the 1964 Declaration of Helsinki and its later amendments. An anaesthesiologist explained the study protocol to the children's parents 1 day before surgery and obtained written informed consent.

Inclusion criteria

Children aged ≤6 yr scheduled for elective surgery under general anaesthesia were eligible.

Exclusion criteria

Children were ineligible if they met any of the following exclusion criteria: American Society of Anesthesiologists (ASA) physical status >2, history of lung resection, history of prematurity, bronchopulmonary dysplasia, or respiratory distress syndrome, abnormal findings on preoperative chest radiography, laparotomy, and laparoscopic surgery.

Anaesthesia

Children were sedated using intravenous thiopental sodium (5 mg kg^{-1}) or propofol (2 mg kg^{-1}). In the operating room, standard monitoring was initiated, including electrocardiography, pulse oximetry, and noninvasive blood pressure measurement, and anaesthesia was induced using sevoflurane 4–6 vol% in 100% oxygen. Following administration of rocuronium 0.6–1 mg kg^{-1} and facemask ventilation for 90 s, patients were intubated with a cuffed tracheal tube (Mallinckrodt™, Dublin, Ireland). Bilateral auscultation was performed to exclude endobronchial intubation.

Mechanical ventilation was started with a V_T of 8 ml kg^{-1} and the ventilatory frequency was adjusted to maintain an end-tidal pressure of carbon dioxide of 4.7–5.3 kPa. The same type of mechanical ventilator (Aisys CS2, GE Healthcare, Milwaukee, WI, USA) was used in all patients. Aisys uses variable orifice flow sensors, which are plastic tubes that have stainless steel flaps. Each side of the flap has a sensor line that is connected to a differential pressure transducer, and differential pressure measurement is converted to the gas flow rate. The inspiratory flow sensor measures the pressure in the breathing system. The inspired oxygen fraction was set at 0.4 and the inspiratory:expiratory ratio was 1:2. Sevoflurane concentration was adjusted to maintain a bispectral index of 40–60. Fentanyl or remifentanil was used for analgesia, at the discretion of the attending anaesthesiologists.

Haemodynamic and respiratory data analysis

Haemodynamic data, including heart rate, blood pressure, and peripheral oxygen saturation, were collected from the patient monitors (Solar™ 8000 patient monitor, GE Healthcare, Lake Forest, IL, USA). Respiratory data were collected from the ventilators. All haemodynamic and respiratory data were transferred to a personal computer using the Vital Recorder program (VitalDB, Korea).[19] Respiratory waveform data were obtained at a sampling rate of 100 Hz through a digital communication system from ventilators and patient monitors. The respiratory system dynamic compliance was calculated using the Vital Recorder program, based on multilinear regression analysis.[20] The driving pressure was calculated as plateau pressure − PEEP.

Study protocol

The intervention was commenced immediately after tracheal intubation. For measurement of the ventilatory parameters, the volume control mode with 20% of inspiratory plateau-pause was maintained during the intervention. PEEP was set to 5, 8, and 12 cm H_2O (hereafter $PEEP_5$, $PEEP_8$, $PEEP_{12}$) according to a randomised order for each patient. The order of PEEP application was determined using a computerized random order list (http://randomization.com). A nurse who was not involved in study intervention prepared the coded, sealed, opaque envelopes containing a card on which the PEEP order written. Attending anesthesiologists opened the envelops and checked the PEEP order. Before applying each PEEP, the recruitment manoeuvre was performed by maintaining a steady airway pressure of 15 cm H_2O with PEEP increments of 5 cm H_2O, with the maximal airway pressure limited to 35 cm H_2O. Each PEEP level was maintained for 5 s. Subsequently, the airway pressure was reduced and returned to the initial ventilator setting. Following the recruitment manoeuvre, each PEEP level was maintained for 15 min to allow equilibration of the respiratory system.[14] The respiratory parameters, including peak inspiratory pressure, mean airway pressure, and end-inspiratory plateau pressure, were measured in the last 5 min at each PEEP level. In addition, the curves of airway pressure, flow, and volume were obtained via the Vital Recorder program.[19] After the 15-min measurement was accomplished, the lungs were collapsed before applying the recruitment manoeuvre and next PEEP level to reset the lung condition. All patients were lying in a supine position during the intervention.

Primary outcome: intratidal compliance profiles

Respiratory waveform data, including volume and pressure graphs over time, were obtained from five consecutive breaths. Using these data, volume-dependent intratidal compliance curves were obtained and categorised using the gliding-SLICE method.[14,18] In detail, the volumes between 5% and 95% were divided into 31 segments, and the compliance was determined via multiple linear regression analysis of data lying within the volume range surrounding the slice by a sixth of the V_T.[16] This calculation was automatically performed via the Vital Recorder program.[19] Using this method, the pressure−volume curve was translated into volume-dependent compliance. The graphs for the intratidal compliance-volume curves were plotted and assessed in Excel (Microsoft Corporation, Redmond, WA, USA).

During mechanical ventilation, the pressure−volume curve has a low inflection point at which recruitment begins and an upper inflection point at which overdistension begins; the V_T should be placed at the linear part between the two points at which compliance is constant and maximal. The interpretation of intratidal compliance profiles has incorporated this concept.[18] At each PEEP level, the gliding-SLICE data within a breath were divided into a lower (0−2.7 ml kg^{-1}), middle (2.7−5.3 ml kg^{-1}), and upper intratidal volume slice (5.3−8 ml kg^{-1}) and the intratidal compliance was calculated at each volume slice. We categorised the curve shape into six specific intratidal compliance profiles (Fig. 1), as previously reported[14,16,18]

I − increasing compliance: indicating recruitment/ derecruitment;
H − horizontal (plateau in compliance, indicating neither recruitment/derecruitment nor overdistension representing the linear part between the lower and upper inflection points in the pressure−volume curve);
IH − increasing compliance before plateau (horizontal), indicating derecruitment in the lower intratidal volume range;
D − decreasing compliance (indicating overdistension);
HD − plateau in compliance (horizontal) followed by decreasing compliance (overdistension in the upper intratidal volume range):
IHD − increasing compliance, followed by plateau (horizontal) and then decreasing (the presence of both recruitment/derecruitment and overdistension in the lower and upper intratidal volume range, respectively).

Secondary outcomes

We assessed the following secondary outcomes:

1. The PEEP level at which optimal PEEP occurred, defined as the PEEP with horizontal profiles based on previous studies.[18,21]
2. Intratidal compliance across three predefined age groups at each PEEP level was compared (infants: 1−12 months; toddlers: 1−3 yr; children: 3−6 yr).

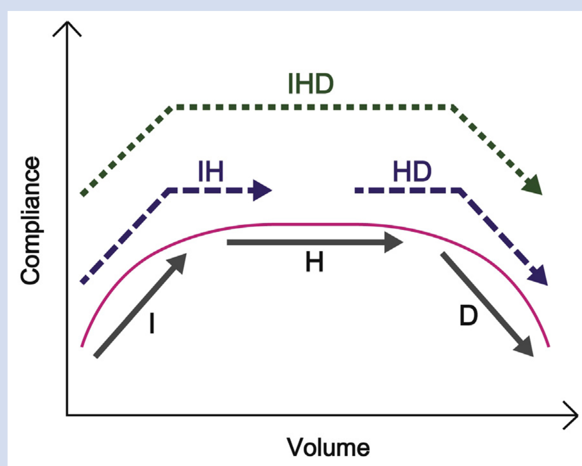

Fig. 1. A schematic drawing of the six compliance profiles classified based on the intratidal compliance−volume curves. H, horizontal compliance profile; I, merely increasing compliance profile; IH, increasing turning into horizontal compliance profile; D, merely decreasing compliance profile; HD, horizontal turning into decreasing compliance profile; IHD, increasing turning into horizontal and further turning into decreasing compliance profile.[16]

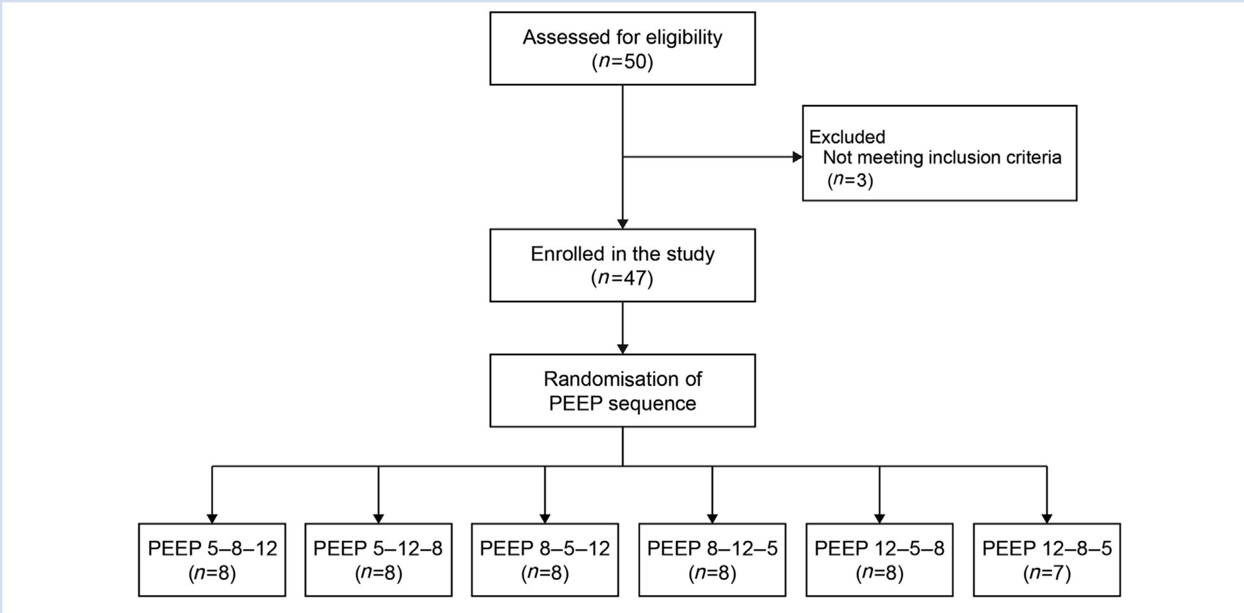

Fig. 2. Study flow chart.

3. Adverse events: episodes of hypotension (defined as blood pressure more than 20% below that at baseline) and perioperative respiratory complications including pneumothorax, respiratory infection, or respiratory distress were recorded.

Statistical analysis

All data were analysed using SPSS for Windows (ver. 23.0; SPSS, Inc., Chicago, IL, USA). Normality of data distribution was assessed using the Shapiro–Wilk's W-test. The differences in the respiratory and haemodynamic parameters among different PEEP levels were compared using one-way repeated measures analysis of variance (ANOVA) with Bonferroni *post hoc* testing. The changes in intratidal dynamic compliance from the lowest to the highest volume slice were analysed using repeated measures ANOVA with Bonferroni *post hoc* testing. The distribution of intratidal compliance profiles among the three PEEP levels was compared using Fisher's exact test. Subgroup analysis for intratidal compliance profile distribution across the three age groups at each PEEP level was performed using the χ^2 test. The original *P* value (0.05) was divided by the number of pairwise comparisons that were performed (corrected *P*-value: 0.05/3=0.017), which was the threshold for statistical significance.

Sample size calculation

The primary outcome of this study was to evaluate the intratidal compliance pattern at different PEEP levels in order to determine the appropriate PEEP level preventing alveolar recruitment/derecruitment and overdistension in children during general anaesthesia. The sample size was obtained by repeated ANOVA using G*Power 3.1 (Universität Kiel, Kiel, Germany) program. As there were no previous studies calculating the effect size, we applied a moderate effect size of 0.25 for the *F*-test presented by Cohen. With an alpha error of 0.05 and a power of 95%, the calculated sample size was 43. Accounting for a 10% attrition rate, the required sample size was set at 47 patients.

Results

Participant characteristics

Of the total 50 patients screened, three patients who did not meet the inclusion criteria were excluded (Fig. 2). Table 1 shows the baseline characteristics of the 47 children randomised to varying PEEP levels. The number of subjects in each random sequence of PEEP level was distributed as follows; *n*=8 in 5–>8–>12, 5–>12–>8, 8–>5–>12, 8–>12–>5, 12–>5->8 and *n*=7 in 12–>8–>5. Two datapoints in two separate subjects could not be analysed owing to poor data quality, resulting in 47 datasets for $PEEP_5$ and 46 datasets for $PEEP_8$ and $PEEP_{12}$, respectively (Fig. 2).

Table 1 Subject characteristics (*n*=47) and type of operation. Data are presented as mean (standard deviation [SD]), median (interquartile range [IQR]; ranges), or absolute number of patients

Age (yr)	2.5 (0.9–3.7; ranges 0.3–6)
Sex (male/female)	28/19
Height (cm)	91.2 (15.6)
Weight (kg)	13.9 (4.2)
Type of surgery	
Plastic surgery	25
Orthopaedic surgery	16
General surgery	5
Urologic surgery	1

Table 2 Ventilatory and haemodynamic parameters during the intervention. Data are presented as mean (SD), median (IQR), or absolute number of patients. Lower intratidal volume, 0–2.7 ml kg^{-1}; middle intratidal volume, 2.7–5.3 ml kg^{-1}; upper intratidal volume, 5.3–8 ml kg^{-1} in the gliding-SLICE data within a breath. H, horizontal compliance profile; I, merely increasing compliance profile; IH, increasing turning into horizontal compliance profile; D, merely decreasing compliance profile; HD, horizontal turning into decreasing compliance profile; IHD, increasing turning into horizontal and further turning into decreasing compliance profile; V_T, tidal volume; VF, ventilatory frequency; PIP, peak inspiratory pressure; P_{plat}, plateau pressure; C_{dyn}, dynamic compliance; C_{stat}, static compliance; BP, blood pressure

PEEP	5 cm H_2O (n=47)	8 cm H_2O (n=46)	12 cm H_2O (n=46)	P-value
Ventilatory parameters				
V_T (ml kg^{-1})	8.3 (0.6)	8.4 (0.5)	8.3 (0.6)	0.222
VF (beats min^{-1})	20 (3)	20 (4)	20 (3)	0.190
PIP (cm H_2O)	13.9 (1.5)	16.3 (1.2)*	20.0 (1.6)*,†	<0.001
Mean airway pressure (cm H_2O)	7.6 (0.5)	10.5 (0.9)*	14.3 (0.5)*,†	<0.001
P_{plat} (cm H_2O)	12.0 (1.5)	14.5 (1.1)*	18.3 (1.1)*,†	<0.001
Driving pressure (cm H_2O)	7.0 (1.5)	6.5 (1.1)	6.3 (1.1)*	0.004
C_{dyn} (ml cm H_2O^{-1})	19.4 (7.0)	20.2 (6.9)	20.8 (7.1)*	0.04
Intratidal compliance profile				
I/IH/H/HD/D/IHD	31/5/5/2/2/2	9/9/16/3/6/3	0/5/9/9/19/4	<0.001
Intratidal dynamic compliance (ml cm H_2O^{-1})				
at lower intratidal volume slice	14.2 (7.2–19.8)	14.8 (9.7–19.8)	16.4 (11.0–22.8)	
at middle intratidal volume slice	17.5 (10.6–21.5)‡	16.2 (9.7–21.1)	15.1 (10.2–21.8)	
at upper intratidal volume slice	19.4 (13.4–26.9)‡,§	16.6 (12.0–21.2)	12.8 (8.1–16.5)‡,§	
Haemodynamic parameters				
Heart rate (beats min^{-1})	139 (18)	140 (18)	140 (17)	0.889
Systolic BP (mm Hg)	91 (13)	90 (12)	88 (12)	0.105
Diastolic BP (mm Hg)	46 (8)	45 (7)	44 (7) *	0.020
Mean BP (mm Hg)	62 (9)	61 (8)	60 (9)	0.055
Spo_2 (%)	99.7 (0.5)	99.8 (0.4)	99.8 (0.4)	0.312

*P value<0.017 when compared with the values at PEEP 5 cm H_2O with Bonferroni correction.
†P value<0.017 when compared with the values at PEEP 8 cm H_2O with Bonferroni correction.
‡P value<0.017 when compared with lower intratidal volume slice with Bonferroni correction.
§P value<0.017 when compared with middle intratidal volume slice with Bonferroni correction.

Study intervention

Peak inspiratory pressure, end-inspiratory plateau pressure, and mean airway pressure increased at higher PEEP levels (Table 2). Dynamic compliance increased and the driving pressure decreased as the PEEP increased from 5 to 12 cm H_2O.

Primary outcome

The intratidal dynamic compliance data at the lower, middle, and upper volume slices within a breath at each PEEP level are shown in Table 2. At $PEEP_5$, the intratidal dynamic compliance increased as the volume increased (P<0.001), whereas at $PEEP_{12}$, it reduced as the volume increased (P<0.001). Conversely, the changes in volume slice level had no influence on the intratidal dynamic compliance at $PEEP_8$ (P=0.415). The distribution of the intratidal compliance profiles differed between different PEEP levels (Fig. 3). At $PEEP_5$, most patients (66%) had increasing compliance. At $PEEP_8$, horizontal (plateaued) compliance (34%) was the most common. At $PEEP_{12}$ decreasing compliance was the most common (41.3%).

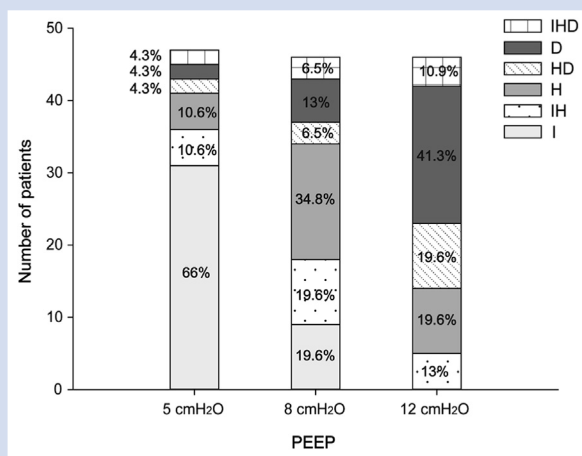

Fig. 3. Distribution of the compliance profiles according to PEEP levels.

Secondary outcomes

Optimal PEEP setting

Optimal PEEP (defined as the PEEP with horizontal profiles based on previous studies)[18,21] occurred across each PEEP level examined (Fig. 4), with $PEEP_8$ being associated with the highest number of horizontal profiles (16/46; 34%). On the assumption that any combination incorporating a horizontal profile provided optimal lung compliance, the highest number of children (28/46; 60.9%) had this profile at $PEEP_8$.

Age-related intratidal compliance

According to the subgroup analysis, intratidal compliance profile distribution was similar among the three age groups at each PEEP level (Supplementary Table S1).

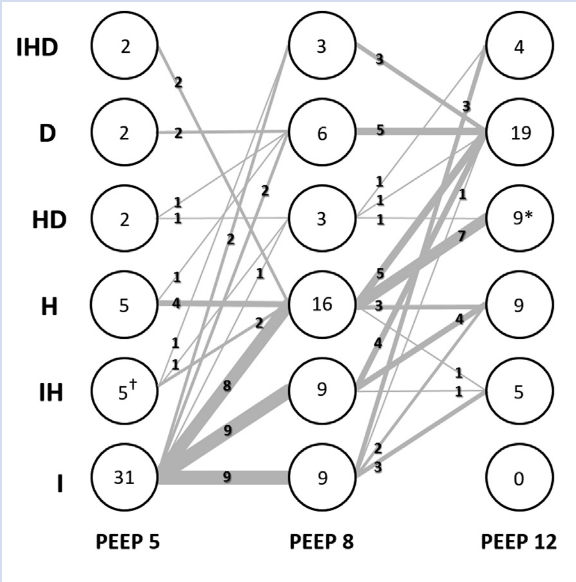

Fig. 4. Individual changes in intratidal compliance profiles with PEEP increase. The numbers inside the circle and on each line represent the number of patients for each intratidal compliance profile and during the profile changes with the increase in PEEP. H, horizontal compliance profile; I, merely increasing compliance profile; IH, increasing turning into horizontal compliance profile; D, merely decreasing compliance profile; HD, horizontal turning into decreasing compliance profile; IHD, increasing turning into horizontal and further turning into decreasing compliance profile. *In one patient, the intratidal compliance profile could not be obtained at PEEP of 8 cm H_2O, but was horizontal to decreasing profile at PEEP of 12 cm H_2O. †In one patient, the intratidal compliance profile could not be obtained at PEEP of 8 cm H_2O, but was increasing to horizontal at PEEP of 5 cm H_2O.

Adverse events

Hypotension did not occur during the PEEP intervention period. There were also no significant perioperative respiratory complications noted.

Discussion

We analysed the intratidal compliance profile at three different PEEP levels in anaesthetised children with healthy lungs. Intratidal derecruitment was most frequently observed at PEEP of 5 cm H_2O and reduced as PEEP increased. At PEEP of 8 cm H_2O, the horizontal compliance profile was the most common pattern. Intratidal overdistension was most frequently observed at PEEP of 12 cm H_2O. Although the intratidal compliance profile varied among the patients, our data suggest that a PEEP level of approximately 8 cm H_2O may be considered most adequate to prevent general anaesthesia-related atelectasis and overdistension.

Data regarding evidence-based guidance for PEEP selection in children is limited. In children, 5 cm H_2O PEEP alone was not sufficient to eliminate general anaesthesia-induced atelectasis.[22] In addition, younger patients more frequently developed atelectasis after induction at PEEP of 5 cm H_2O.[22] According to a recent prospective randomised trial performed in children undergoing pulmonary resection, low V_T with 6 cm H_2O PEEP reduced postoperative pulmonary complications when compared with moderate V_T without PEEP.[7] However, it was not associated with long-term outcome improvement.[7]

A recent study in adults found that the PEEP required to prevent both atelectasis and overdistension varies widely among patients during anaesthesia.[23] Optimal PEEP may be determined using electrical impedance tomography[23] or by minimising driving pressure.[13] We determined the optimal PEEP level using intratidal compliance profile analysis.[10,12,14] Our study is the first to analyse the intratidal compliance-volume relationship in children during intraoperative mechanical ventilation with different PEEP levels higher than 5 cm H_2O. Weber and colleagues[21] showed that individualised PEEP titrated according to intratidal respiratory compliance profiles improved regional ventilation without affecting impedance distribution. Wirth and colleagues found that a PEEP of 5 cm H_2O during intraoperative mechanical ventilation could not prevent intratidal derecruitment both in adults[16] and children[11] after obtaining intratidal compliance profiles of each patient.

Intratidal compliance profile analysis using the gliding-SLICE method detects intratidal recruitment and overdistension and to help maintain lung-protective mechanics.[12,13] Using this method, we found that alveolar ventilation patterns, intratidal recruitment/derecruitment, overdistension or combined, can be estimated based on the intratidal compliance profile in paediatric patients. However, these profiles at certain PEEP levels in children appear to vary more than in adult patients.[14] Specifically, in adults studied, none had a decreasing intratidal compliance profile component (including D, HD, or IHD profiles), regardless of the PEEP levels when V_T was 8 ml kg^{-1}.[14] By contrast, there were D, HD, and IHD profiles at all PEEP levels in our patients. These data suggest that V_T of 8 ml kg^{-1} might cause intratidal overdistension in paediatric patients, particularly when combined with a higher PEEP level. Applying a low V_T can improve the intratidal compliance profiles. Low V_T may be beneficial in children who have a D component in the intratidal compliance profile when PEEP is increased. For example, it is necessary to increase PEEP to prevent atelectasis in children with an I component in the intratidal compliance profile. However, if PEEP is increased with the same V_T, a D component may develop in the intratidal compliance profile, such as HD or IHD. In this case, lowering the V_T while increasing the PEEP may be beneficial.

As we obtained flow, pressure, and volume curves in real time to calculate intratidal compliance, this enabled best PEEP to be applied throughout the perioperative period. We found that the intratidal compliance remained stable as the volume increased at PEEP of 8 cm H_2O. The horizontal intratidal compliance profile was most commonly observed in patients at this PEEP level. At PEEP of 5 cm H_2O, the intratidal compliance significantly increased as the volume increased, suggesting that ventilation took place at a lower inflection point of the pressure–volume relation curve, indicating recruitment/derecruitment. In contrast, the intratidal compliance decreased as the volume increased at PEEP of 12 cm H_2O, suggesting that ventilation occurred at the upper inflection point, indicating overdistention.[17] Considering that the driving pressure was similarly low both at PEEP of 8 and 12 cm H_2O, the intratidal compliance profile can provide a more specific method to determine the more appropriate PEEP level. From our study, we suggest that a PEEP above that commonly used or recommended (3–5 cm H_2O),[24] would be necessary to avoid alveolar collapse in most paediatric patients undergoing general anaesthesia.

Several limitations to this study should be highlighted. First, we applied a V_T of 8 ml kg^{-1} based on the actual, not predicted body weight. Predicted body weight is recommended for LPV for children.[25] However, according to Imber and colleagues,[26] although the V_T normalised to the ideal body weight was larger than that normalised to the actual body weight, the median V_T was similar. Second, we did not evaluate atelectasis and overdistension quantitatively or by lung regions using other tools, such as thoracic impedance tomography.[14] Thoracic impedance tomography would allow assessment of the proportion of recruited, collapsed, or overdistended regions, as well as a better respiratory mechanics evaluation. However, the regional heterogeneity of the lungs could not be evaluated in this study owing to the lack of thoracic impedance tomography. Third, we could not exclude the tracheal tube resistance during measurement of respiratory system compliance. Finally, we applied a fixed V_T during the evaluation of intratidal compliance profile. The profile can be different according to both PEEP level and V_T. Further research is needed to determine the best PEEP and optimal V_T for obtaining an ideal intratidal compliance profile. In addition, it is necessary to investigate whether the gliding-SLICE method enables predicting changes in respiratory mechanics after a certain PEEP change and improving clinical outcomes after surgery.

In conclusion, this study evaluated the intratidal compliance profile at different PEEP levels higher than 5 cm H_2O in children undergoing general anaesthesia. At PEEP of 8 cm H_2O, the majority of children could avoid both atelectasis and overdistension. However, there was a large interindividual variability among the patients regarding the appropriate PEEP. Thus, a PEEP greater than that commonly used in clinical settings would be necessary to avoid alveolar collapse in most paediatric patients undergoing general anaesthesia. Further studies should focus on determining the best PEEP using intratidal compliance profiles and its association with long-term outcomes in mechanically ventilated, critically ill children, and children undergoing surgery.

Authors' contributions

Study conception and design: JHL, JTK
Data acquisition: SHJ, EHK, JTK, JHL
Data analysis and interpretation: YEJ, HCL, JHL
Writing paper: JHL, SHJ
Revising paper: SHJ, JTK, HSK
All authors participated in critical revision of the manuscript for important intellectual content, and gave final approval

Declarations of interest

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.06.046.

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