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Measurement of end-expiratory lung volume in intubated children without interruption of mechanical ventilation

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Abstract Purpose: Monitoring end-expiratory lung volume (EELV) is a valuable tool to optimize respiratory settings that could be of particular importance in mechanically ventilated pediatric patients. We evaluated the feasibility and precision of an intensive care unit (ICU) ventilator with an in-built nitrogen washout/washin technique in mechanically ventilated pediatric patients. **Methods:** Duplicate EELV measurements were performed in 30 patients between 5 kg and 43 kg after cardiac surgery (age, median + range: 26, 3–141 months). All measurements were taken during pressure-controlled ventilation at 0 cm H₂O of positive end-expiratory pressure (PEEP). **Results:** Linear regression between duplicate measurements was excellent ($R^2 = 0.99$). Also, there was good agreement between duplicate measurements, bias \pm SD: -0.3% (-1.5 mL) \pm 5.9% (19.2 mL). Mean EELV \pm SD was 19.6 ± 5.1 mL/kg at 0 cm H₂O PEEP. EELV correlated with age ($p < 0.001$, $r = 0.92$, $R^2 = 0.78$), body weight ($p < 0.001$, $r = 0.91$, $R^2 = 0.82$) and height ($p < 0.001$,

$r = 0.94$, $R^2 = 0.75$). **Conclusion:** This ICU ventilator with an in-built nitrogen washout/washin EELV technique can measure EELV with precision, and can easily be used for mechanically ventilated pediatric patients.

Keywords Functional residual capacity · Pediatric · Positive-pressure respiration · Lung volume measurements · Anesthesiology

Abbreviations

| | |
|------------------|----------------------------------|
| CPB | Cardiopulmonary bypass |
| EELV | End-expiratory lung volume |
| FiO ₂ | Fraction of inspired oxygen |
| ICU | Intensive care unit |
| NMBW | Multiple breath nitrogen washout |
| PEEP | Positive end-expiratory pressure |
| RCM | Recruitment maneuver |
| TEE | Transesophageal echocardiography |

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Introduction

Monitoring end-expiratory lung volume (EELV) might be a valuable tool to optimize respiratory settings in anesthetized ventilated patients [1]. General anesthesia is

known to promote lung volume reduction, which promotes atelectasis, lung compliance, and arterial oxygenation [2]. In children, decreased lung volume is of special importance because of the lower elastic retraction forces and a lower relaxation volume, which makes them

more prone to airway collapse [3, 4]. Furthermore, EELV has been described as one of the variables known to adequately assess mechanical characteristics of the ventilated lung [5].

However, determining EELV in ventilated patients is not without difficulty. EELV can be measured with computer tomography [6, 7], but this technique is not available for routine measurements. Traditionally, EELV measurement techniques are based on dilution of tracer gases, like sulfur hexafluoride washout [8, 9], closed-circuit helium dilution [10], or open-circuit multibreath nitrogen washout [11–13]. All these techniques require expensive and/or complex instrumentation, and are generally not suitable for routine EELV measurements during surgery and in the intensive care unit (ICU). An alternative is the simplified helium dilution method, using a re-breathing bag with a helium mixture. However, an important disadvantage of this latter technique is the interruption of mechanical ventilation for a short period of time [14].

Recently, Stenqvist et al. [15] introduced a novel method to measure EELV without interruption of mechanical ventilation, based on a simplified and modified multiple Breath nitrogen washout (MBNW) technique, which is integrated within a mechanical ventilator. This method requires a step change in the inspired oxygen fraction (FiO_2), without the need for supplementary tracer gases or specialized additional monitoring equipment [15]. Although this method has been successfully applied in adult ventilated patients at the ICU and whilst undergoing surgery [15–17], no data regarding feasibility and precision exist for mechanically ventilated pediatric patients.

Therefore, we evaluated the feasibility and precision of this MBNW device to measure EELV during mechanical ventilation of pediatric patients after cardiac surgery.

Methods

After approval of the local institutional human investigations committee, 30 mechanically ventilated children were enrolled in the study. All patients underwent cardiac surgery for congenital heart repair, and received postoperative mechanical ventilatory support in the ICU. Exclusion criteria were: severe cardiovascular instability, thoracic deformations, and residual intracardiac shunt postoperatively evaluated by transesophageal echocardiography (TEE).

EELV measurements were carried out with the COVX module (GE Healthcare, Helsinki, Finland) integrated within the ventilator. This module has been described in detail earlier [15]. Briefly, O_2 and CO_2 are measured with standard clinical sensors and the residual N_2 as remaining

ventilator air is calculated. A step change in the N_2 concentration is induced by changing the FiO_2 . The N_2 volume change and N_2 fraction change is measured with the COVX module integrated in the Engström Carestation ventilator and EELV is calculated.

Patients were nasotracheally intubated with a cuffed Hi-Contour pediatric endotracheal tube (Mallinckrodt) and anesthesia was maintained with midazolam 0.1 mg/(kg h) and sufentanil 1 mcg/(kg h). During the operation, patients were ventilated in pressure-controlled mode at the following settings: tidal volume of 6–8 mL/kg, frequency adjusted to maintain a PaCO_2 level between 4.5 and 5.5 kPa, positive end-expiratory pressure (PEEP) of 8 cm H_2O , I/E ratio of 1:1 and FiO_2 of 0.5. After weaning from cardiopulmonary bypass (CPB), the lungs were routinely re-expanded by a recruitment maneuver (RCM) and mechanical ventilation was continued with the same settings as before CPB. Once admitted to the ICU, mechanical ventilation was continued with the same settings as before transportation except for the FiO_2 , which was set at 0.40 or 0.45. FiO_2 was decreased because the measurement requires a FiO_2 step change and becomes less precise at a FiO_2 above 0.65, according to manufacturer's specifications. Patients were sedated by midazolam intravenously [0.1 mg/(kg h)] and morphine [10 mcg/(kg h)].

After stabilization at the ICU, EELV was measured twice (washout and washin) with the COVX module by nitrogen washout/washin with first an incremental and second a decremental FiO_2 step of 0.2 at a PEEP of 0 cm H_2O . This measurement was repeated after 10 min. Before measurements, hemodynamic and ventilatory parameters were recorded and arterial blood gas analysis was performed.

Statistical analysis

Statistical analysis was performed with Graphpad software package (version 5.0, Graphpad Software Inc., San Diego, USA). Results are expressed as mean \pm SD for normally distributed data and median and interquartile range (IQR) for not normally distributed data. The Shapiro–Wilk normality test was used to evaluate the distribution of all data. Agreement between duplicate measurements was analyzed using Spearman correlation and Bland–Altman's analysis [18]. For all comparisons, $p < 0.05$ was considered significant.

Results

In the present study, 30 mechanically ventilated patients were examined; Table 1 presents demographic data and the main physiologic characteristics. All patients were

Table 1 Characteristics of the patient population

| | |
|-----------------------|-------------|
| N | 30 |
| Gender, female/male | 9/21 |
| Age in months (range) | 26 (3–141) |
| Weight (kg) | 10.9 (8.5) |
| Height (m) | 0.87 (0.35) |

Data are presented as median with interquartile range unless stated otherwise

Table 2 Hemodynamic and ventilatory parameters before EELV measurement

| | |
|--------------------------------|-------------|
| Heart rate (bpm) | 124 (22) |
| Mean arterial pressure (mm Hg) | 65 (11) |
| FiO ₂ (%) | 41 (2) |
| Tidal volume (mL/kg) | 7.7 (1.0) |
| pH | 7.41 (0.05) |
| PaO ₂ (kPa) | 20.7 (7.3) |
| PaCO ₂ (kPa) | 4.38 (0.46) |
| SaO ₂ (%) | 98.4 (2.4) |

Data are presented as mean with standard deviation unless stated otherwise

studied after congenital cardiothoracic surgery and tolerated the procedure well. Repairs included closure of ventricular septal defect (7), closure of atrial septal defect (8), correction of tetralogy of Fallot (3), repair of subpulmonary stenosis (3) and subaortic stenosis (2), pacemaker implantation (1), and total cavopulmonary connection (6). The hemodynamic and ventilatory parameters before the measurements at 0 cm H₂O PEEP are provided in Table 2.

Linear regression between duplicate EELV measurements (as average of washin/washout) measured with the nitrogen washin/washout technique was performed. Duplicate measurements were highly correlated ($p < 0.001$, $r = 0.99$, $R^2 = 0.99$). To assess the difference between the duplicate measurements a Bland–Altman analysis was performed (Fig. 1). Bias \pm SD was -0.3% (-1.5 mL) \pm 5.9% (19.2 mL).

Mean EELV \pm SD was 19.6 ± 5.1 mL/kg at a PEEP level of 0 cm H₂O. Figure 2 shows the relation between EELV and patient characteristics. EELV was highly correlated with age ($p < 0.001$, $r = 0.92$, $R^2 = 0.78$), body weight ($p < 0.001$, $r = 0.91$, $R^2 = 0.82$) and height ($p < 0.001$, $r = 0.94$, $R^2 = 0.75$).

Discussion

The present study shows that, in sedated mechanically ventilated pediatric patients, this noninvasive MBNW technique can easily measure EELV with good precision. We confirmed that EELV is highly correlated with the patient's height and body weight (Fig. 2).

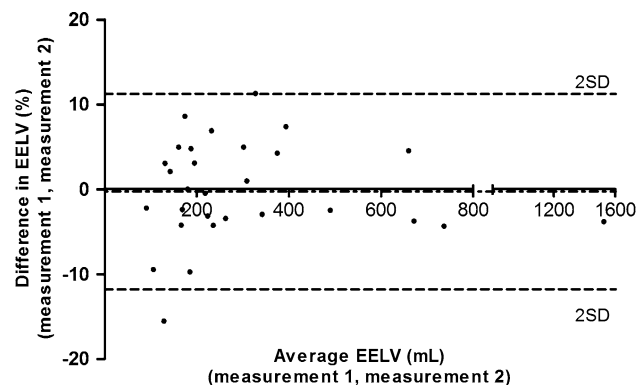


Fig. 1 Bland–Altman analysis. Comparison of duplicate end-expiratory lung volume (EELV) measurements with the multibreath nitrogen washout technique. Measurements were performed in the supine position at 0 cm H₂O positive end-expiratory pressure (PEEP) in mechanically ventilated pediatric patients after cardiac surgery

Precise and easily performable measurements of EELV are essential in order to use this parameter to optimize respiratory settings. Although accurate and precise methods to measure EELV are available for ventilated pediatric patients, these older methods require complex equipment or tracer gases that limit their use in clinical practice [8, 19]. In this study, we used an ICU ventilator with an in-built MBNW technique to measure EELV during mechanical ventilation; a good agreement was found between duplicate measurements with this device. Chiumello et al. [20] recently compared this technique with computed tomography and helium dilution in adult ICU patients and described high reproducibility between duplicate measurements (bias \pm SD 48 ± 165 mL). In our pediatric patients an even better level of precision was found: bias \pm SD 1.0% (-1.7 mL) \pm 5.7% (15.5 mL).

Although accuracy was not evaluated in the present study, measured EELV was comparable to that reported in other studies [21–24]. Ungern-Sternberg et al. [24] described the effect of CPB and aortic clamping on EELV in children during mechanical ventilation with 3 cm H₂O PEEP; in their study EELV increased from 22 ± 5 to 27 ± 6 mL/kg after opening of the chest and decreased markedly to 16 ± 5 mL/kg after closing the chest and was still reduced to 18 ± 5 mL/kg during the following 90 min. These values are comparable with our measured EELV (mean \pm SD) of 19.6 ± 5.1 mL/kg. Moreover, our values are similar to those of pediatric patients during nitrous-oxide-halothane anesthesia, in which an EELV (mean \pm SD) of 19 ± 6 mL/kg was found during mechanical ventilation and 22 ± 7 mL/kg during spontaneous breathing [22].

Schibler et al. [25] investigated the effect of different levels of PEEP on EELV in 22 mechanically ventilated children. At 0 cm H₂O PEEP, EELV was 20 ± 7 mL/kg, which is comparable to our results. At a PEEP of 5 and 10 EELV increased to 24 ± 8 and 28 ± 6 mL/kg,

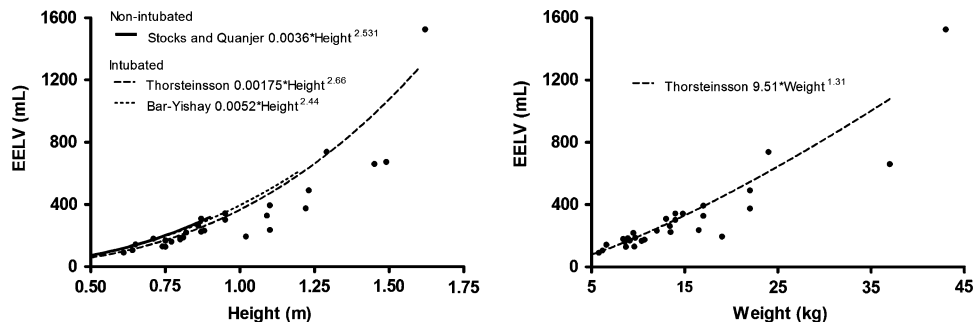


Fig. 2 Relation between EELV (average of duplicates) and height or body weight. Measurements were performed in the supine position at 0 cm H₂O PEEP in mechanically ventilated pediatric patients after cardiac surgery. The *lines* represent non-linear

regression equations from non-intubated children, Stocks and Quanjer [26] and intubated children at 0 cm H₂O PEEP, Thorsteinsson et al. [23] and Bar-Yishay et al. [21]

respectively. In the present study, we did not use PEEP during the measurements to allow comparison to studies in which EELV was measured without PEEP [21, 23, 26]. The application of PEEP is known to increase EELV and to prevent the formation of atelectasis. If higher PEEP levels were used, the EELV could be restored to above the normal values displayed in Fig. 2.

Among our patients, characteristics such as age, height, and body weight were highly correlated with measured EELV (Fig. 2). Our data are comparable with data from two previous studies [21, 23] in which children were ventilated without the application of PEEP. Below 1 m of height or below 15 kg body weight, the agreement was excellent, but above 1 m of height most of our values were slightly below their regression equations. The reason for this is unknown. Thorsteinsson et al. [23], measured EELV directly after induction of anesthesia in healthy children and in children with cardiac anomalies, whereas we measured EELV after cardiac surgery with CPB. It is known that cardiac surgery and CBP may lower EELV [24, 27]. Bar-Yishay et al. [21], measured EELV in awake children in the supine position or during ketamine anesthesia. Ketamine anesthesia is known to preserve lung function [28].

A potential limitation of the present study is that accuracy was not evaluated. However, measured values with this technique were close to those of previous

studies. Another potential limitation of the used technique is the measurement of EELV in patients requiring a FiO₂ >65%. It has been suggested in the manufacturer's specifications that the accuracy error increases from 10% to 15% at a FiO₂ >0.65 in adult patients. However, in the present study we only measured at a FiO₂ <65%. An important advantage of this method is that no tracer gases and no expensive or specialized equipment are required, bringing this parameter closer to clinical practice.

Therefore, we conclude that this nitrogen washout EELV technique can measure EELV with good precision. Especially below a height of 1 m or 15 kg body weight, our data are in good agreement with earlier comparable studies. Furthermore, this device can easily be used in mechanically ventilated pediatric patients without a tracer gas and without interruption of mechanical ventilation.

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