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Comparison of four methods for measuring elevation of FRC in mechanically ventilated infants

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Abstract The aim of the study was to compare measurements of the elevation of functional residual capacity (FRC) above the relaxation volume obtained in 34 mechanically ventilated infants (median weight 2.6 kg, range 1.2–9) from four different methods: (1) direct measurement of the complete exhalation volume after brief disconnection from the ventilator, (2) calculated measurement from total positive end-expiratory pressure (PEEP) measured by end-expiratory occlusion of the breathing circuit, (3) extrapolated evaluation from the mathematical model of Brody, (4) extrapolated evaluation from the passive expiration method. We considered the direct measurement (1) as the "gold standard". Measurements obtained by total PEEP (2) and by the Brody's mathematical model (3) provided similar results than the direct measurement. Conversely, graphical extrapolation from the passive expiration method (4) underestimated the elevation of FRC. In conclusion, we suggest using the mathematical extrapolation from the Brody's model to evaluate the elevation of FRC in mechanically ventilated infants: this method is non-invasive, does not require disruption of gas flow, can be easily performed with all the neonatal ventilators, and allows continuous breath-by-breath measurements.

Key words Respiratory mechanics · Mechanical ventilation · Infants · End-expiratory lung volume · Dynamic elevation of FRC

Introduction

Conventional mechanical ventilation is frequently required to manage respiratory failure in infants. Addition of a positive end-expiratory pressure generated by the ventilator (PEEPv) is usually needed to improve oxygenation [1, 2]. This PEEPv increases the lung volume at the end of expiration, i.e., the functional residual capacity (FRC) [3, 4]. During mechanical ventilation in infants, other mechanisms also increase FRC above the elastic equilibrium volume of the total respiratory system, i.e. the relaxation volume (EELV). Dynamic elevation of FRC occurs when expiratory time is shorter than the time required to achieve a complete exhalation and may thus result from: (1) expiratory time less than three time constants of the respiratory system, (2) increased time constant of the respiratory system in the case of increased flow resistance or compliance, (3) increased tidal volume if expiratory time is too short. As high respiratory frequency with short expiratory time has been recommended to decrease lung barotrauma/ volutrauma [5], dynamic elevation of FRC can occur in mechanically ventilated infants. Its presence implies that alveolar pressure remains positive throughout expiration. This positive end-expiratory alveolar pressure, not generated by the ventilator, has been termed auto or

intrinsic positive end-expiratory pressure (PEEPi). The difference between FRC and the relaxation volume represents the elevation of FRC (ΔEELV) by both PEEPv and dynamic factors leading to the development of PEEPi.

Evaluation of ΔEELV generated by PEEPv and/or PEEPi is a fundamental issue in mechanically ventilated infants, as lung distension may impair respiratory function. Pulmonary hyperinflation decreases lung compliance [6, 7] and may increase pulmonary vascular pressure and resistance [8]. Although ventilation at low lung volume may induce lung injury by repeated collapse and reinflation of the terminal airways, pulmonary hyperinflation may also increase volutrauma and thus the risk of chronic lung disease [9, 10], especially in premature newborn infants.

ΔEELV is usually estimated from end-expiratory alveolar pressure measurement [6, 11]. Indeed, theoretically, ΔEELV is the product of end-expiratory alveolar pressure by compliance of the respiratory system. However, estimation of ΔEELV from end-expiratory alveolar pressure may be not reliable, as expiratory muscle activity can alter end-expiratory alveolar pressure. Furthermore, end-expiratory alveolar pressure measurement requires an end-expiratory occlusion device in the breathing circuit that is not available in most neonatal ventilators. Another method is based on the measurement of total exhaled volume during a period of apnea obtained by disconnecting the Y-piece from the ventilator [12, 13]. This total exhaled volume represents the volume of the lung above FRC at the end of tidal inspiration. ΔEELV can be calculated as the difference between total exhaled volume and tidal expiratory volume (Vte). However, this method of direct ΔEELV measurement requires disconnection from the ventilator and may be not well tolerated. Therefore, there is a need to develop an easy and reliable method to measure the end-expiratory trapped gas volume in mechanically ventilated infants.

Two other methods for quantifying ΔEELV have been described [14–16]. These methods are based on mathematical extrapolation from tidal flow and volume recordings and do not require end-expiratory occlusion and disconnection from the ventilator.

The purpose of this study was to compare, in a group of mechanically ventilated infants, these four methods of ΔEELV measurement. We considered the direct ΔEELV measurement to be the reference method.

Patients and methods

Population

Thirty-four infants (gestational age 28–39 weeks; median postnatal age 4 days, range 1–211 days; median weight 2.6 kg, range 1.2–9 kg) were enrolled in the study after permission was obtained from their parents. Twenty-five infants were admitted for the management of respiratory failure (bronchopulmonary dysplasia 11, hyaline membrane disease 8, bronchiolitis 6). Nine infants were mechanically ventilated for neurologic disorders and had no pulmonary disease. All infants were intubated with an uncuffed endotracheal tube (Portex) and connected via a short rigid tube (60-cm length; 1-cm internal diameter) to a Servo 900C ventilator (Siemens-Elema, Solna, Sweden) set in the volume-controlled constant-flow mode. In order to reduce compressible volume, the usual heater humidifier was replaced by a "heat and moisture exchanger" (dead space 0.6 ml, flow resistance 4.4 cm H_2O/l per s, Neonate Hygroflux, Vygon, France). Flow was measured by a pneumotachometer (Fleisch no. 00) and a differential pressure transducer (Validyne ± 2 cm H_2O, USA) placed between the endotracheal tube and the Y-piece of the ventilator circuit. Although the pneumotachometer was not heated, risk of water condensation on the screen was low because the infants and the pneumotachometer were placed inside a closed incubator (temperature above 34 °C). Apparatus dead space (pneumotachometer and connector) was 2 ml. Volume was obtained by analog integration of the flow signal. Airway pressure was recorded at airway opening with another pressure transducer (Validyne ± 50 mm Hg, USA). All variables were simultaneously displayed on a four-channel polygraph (Linseis, Germany). Flow-volume (V′/V) and pressure-volume loops were recorded on a X/Y table (Hewlett-Packard, USA). The tests were performed in the supine position during quiet sleep. The infants were sedated with diazepam (0.5 mg/kg) and nalbuphine (0.2 mg/kg) and were fully ventilated. Tracheal suction was performed immediately before each test. Impairment of hemodynamic or respiratory parameters was not observed.

Respiratory mechanics measurements

Static compliance (Cstat,rs) and total resistance (Rtot,rs) of the respiratory system and total PEEP (PEEPt) were measured by using the occlusion method described by Bates et al. [17]. Briefly, airways were occluded at the end of inflation and at the end of expiration for 3 to 4 s by using the end-inspiratory and end-expiratory pause buttons of the ventilator: air leaks were suspected if plateau pressure could not be obtained. In that case, a gentle pressure was applied on the trachea. Furthermore, a stable plateau pressure provided evidence of relaxation of the respiratory muscles as well as equilibration between alveolar and airway pressure. If a stable plateau pressure could not be obtained, the infant was not enrolled in the study. Volume and pressure-time curves and V′/V loops were analyzed. It was verified on the volume-time curve that occlusion started just at the end of inflation or expiration and on the V′/V loop that flow was constant during all the inspiratory time. Three to five ventilatory cycles were recorded to ensure reproducibility. End-inspiratory airway occlusion was characterized by a rapid initial drop in airway pressure from peak inspiratory pressure (PIP) to P1, then followed by a slower decrease in pressure that reached an apparent plateau value (Pplat). The slope of the linear portion of Pplat was extrapolated until the end-inspiratory time to evaluate Pplat, assumed to represent the elastic recoil pressure of the total respiratory system at end-inspiration. End-expiratory airway occlusion was followed by a gradual increase of the pressure to an apparent plateau value PEEPt. PEEPt represented the elastic recoil pressure of the total respiratory system at end-expiration. Cstat,rs of the respiratory system was calculated as follows:

$$Cstat,rs = Vte/(Plat - PEEPt)$$

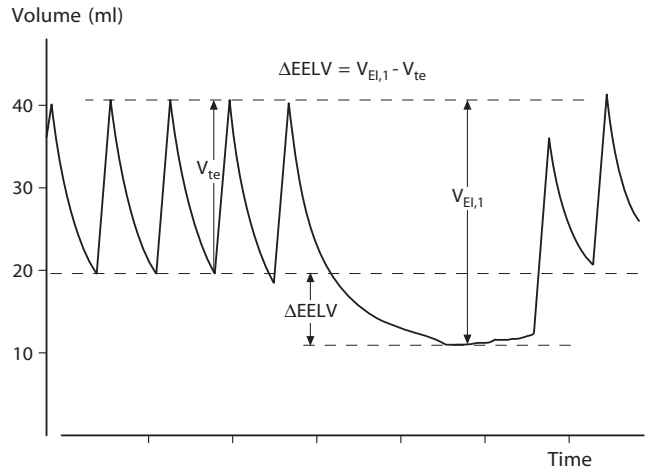


Fig. 1 Direct measurement of lung volume above elastic equilibrium volume ($\Delta EELV_1$). Total exhaled volume $V_{EI,1}$ was measured during expiration after the Y-piece of the breathing circuit was disconnected from the ventilator for 4 s. $\Delta EELV_1$ was evaluated as the difference between $V_{EI,1}$ and tidal expiratory volume *Vte*

Rtot,rs was calculated by dividing the difference between PIP and Pplat by the constant inspiratory flow V'_i ($V'_i = V_{ti}/T_i$: V_{ti} = tidal volume; T_i = inspiratory time) preceding the occlusion:

$$Rtot,rs = (PIP - Pplat)/V'_i$$

Measurements of ΔEELV

Direct measurement (Fig. 1)

$\Delta EELV_1$ was quantified by measuring the total exhaled volume during expiration after the Y-piece of the breathing circuit was disconnected from the ventilator for 4 s [12, 13]. This total exhaled volume represented the volume of the lung above FRC at the end of tidal inspiration ($V_{EI,1}$). The difference between $V_{EI,1}$ and Vte represented the lung volume above FRC at the end of tidal expiration (Fig. 1):

$$\Delta EELV_1 = V_{EI,1} - Vte$$

Calculation of ΔEELV from total PEEP (Tuxen's method) (Fig. 2)

PEEPt was measured by using an end-expiratory airway occlusion [18–20]. By assuming a constant compliance of the respiratory system (Crs,stat) within the tidal volume, $\Delta EELV_2$ can be evaluated as follows:

$$\Delta EELV_2 = Cstat,rs \times PEEPt$$

Mathematical or graphical extrapolations

1. Mathematical extrapolation from Brody's model [14, 15]

If $V_{EI,3}$ represents the volume above FRC at the end of tidal inspiration, the difference between $V_{EI,3}$ and Vte can be written as:

$$V_{EI,3} - Vte = V_{EI,3}\, e - T_{e/\tau rs}$$
$$\text{and } V_{EI,3} = Vte/(1 - e - T_{e/\tau rs})$$

where Te is the expiratory time, and τrs is the time constant of the respiratory system estimated from the slope of the expiratory part of the V′/V curve (Fig. 3). Then, $\Delta EELV_3$ can be calculated:

$$\Delta EELV_3 = V_{EI,3} - Vte$$

2. Graphical extrapolation from the flow/volume loop (Fig. 3)

$\Delta EELV_4$ was estimated by analyzing the tidal V′/V loop [16]. The slope of the linear part of the expiratory V′/V relation was extrapolated up to zero flow level to evaluate $V_{EI,4}$. In the case of incomplete expiration, $V_{EI,4}$ represents the sum of Vte and $\Delta EELV_4$:

$$\Delta EELV_4 = V_{EI,4} - Vte$$

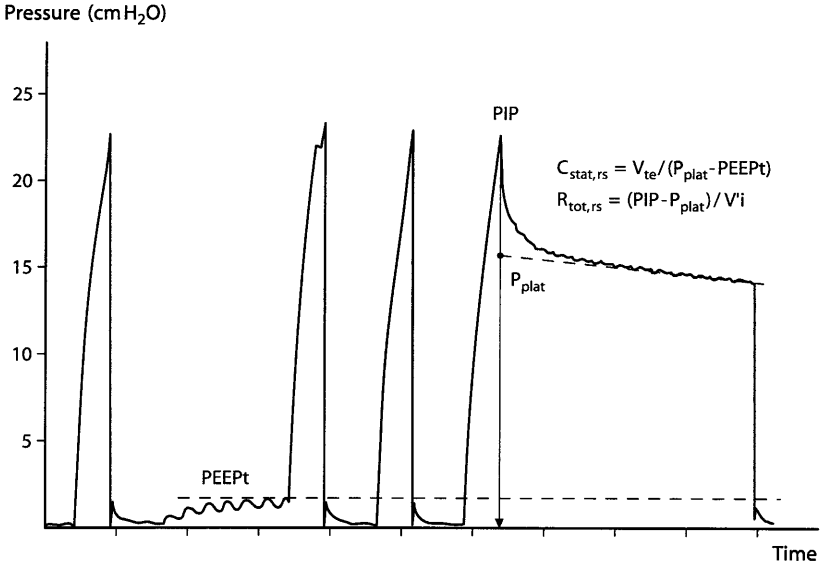


Fig. 2 Calculation of lung volume above elastic equilibrium volume ($\Delta EELV_2$) from total PEEP measurement (Tuxen's method). After the end-expiratory occlusion of the breathing circuit, airway pressure increases to a plateau pressure considered as total PEEP *PEEPt*. $\Delta EELV_2$ was calculated as the product of static compliance of the respiratory system *Cstat,rs* by PEEPt. *PIP* peak inspiratory pressure, *Pplat* plateau pressure

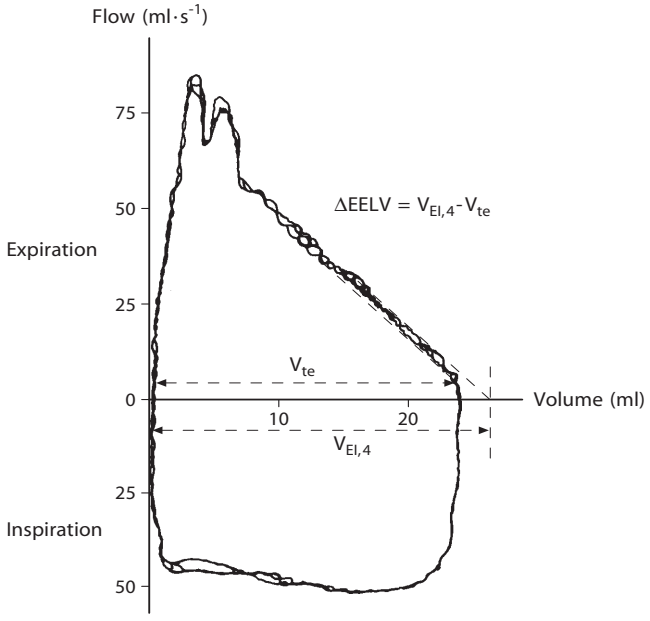


Fig. 3 Graphical extrapolation from the tidal flow/volume loop (passive expiration method): the slope of the linear part of the expiratory flow/volume loop was extrapolated up to zero flow to evaluate the volume above EELV at the end of tidal inspiration $V_{EI,4}$. $\Delta EELV_4$ was calculated as the difference between $V_{EI,4}$ and Vte

Statistical analysis

Results are expressed as mean ± SD. $\Delta EELV_2$, $\Delta EELV_3$, and $\Delta EELV_4$ were compared to $\Delta EELV_1$ by using linear regression, the method of Bland and Altman [21], and dependent two-tailed *t*-test. The degree of agreement was summarized by calculating the mean difference and the standard deviation of the differences (SD). If differences within the limits of agreement, i. e. mean difference ± 2 SD, were not clinically important, the methods were considered interchangeable. A *p* value at 0.05 was considered significant.

Results

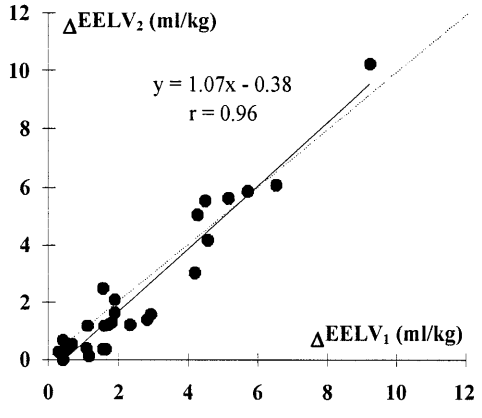
Characteristics of the population studied and ventilator settings are shown in Table 1. $\Delta EELV_1$ was higher in infants with bronchopulmonary dysplasia and bronchiolitis than in infants with hyaline membrane disease or without parenchymal disease ($p < 0.05$) and may represent more than 30 % of the tidal volume (Table 1).

A significant correlation was observed between individual values obtained by direct measurement ($\Delta EELV_1$) and those obtained from total PEEP (Tuxen's method) ($\Delta EELV_2$) and from mathematical extrapolations (Brody's model) ($\Delta EELV_3$) (Figs. 4, 5). Conversely, despite a significant correlation, ΔEELV evaluated from the graphical extrapolation method ($\Delta EELV_4$) was lower than $\Delta EELV_1$ (Fig. 6). A good agreement was observed by the Bland and Altman method [21] between direct measurement ($\Delta EELV_1$) and calculated ($\Delta EELV_2$) or extrapolated measurement from the Brody's model ($\Delta EELV_3$) [95 % confidence interval (CI): $\Delta EELV_1 - \Delta EELV_2 = 0.22$ ml/kg, $\Delta EELV_1 - \Delta EELV_3 = 0.19$ ml/kg] (Figs. 4, 5). In contrast, the comparison between $\Delta EELV_1$ and $\Delta EELV_4$ showed a wide 95 % CI, reflecting a lack of agreement between the two methods (95 % CI $\Delta EELV_1 - \Delta EELV_4 = 0.38$ ml/kg) (Fig. 6).

Discussion

In this study, elevation of FRC (ΔEELV) during mechanical ventilation was measured by using four different methods in 34 infants. We found that measurements

Fig. 4 Comparison between direct measurement and calculation from total PEEP (Tuxen's method) of the volume above EELV at end-expiration by correlation, *dotted line* line of identity, *dashed line* regression line, and Bland and Altman analysis (difference ± 2 SD against mean)



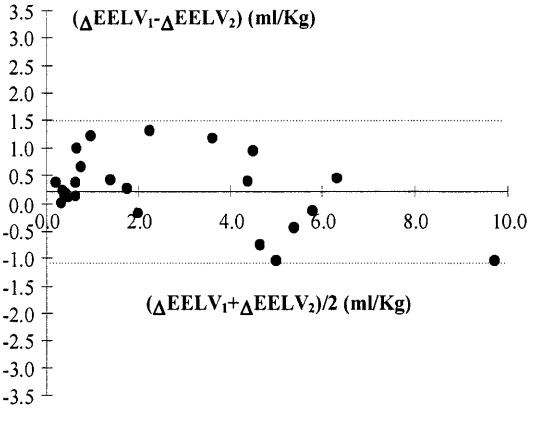


Table 1 Characteristics of the population studied. Values are mean ± SD (*HMD* Hyaline membrane disease, *BPD* bronchopulmonary dysplasia, FIO_2 fractional inspired oxygen, *Vte* tidal expiratory volume, *PIP* peak inspiratory pressure, $PEEP_V$ positive end-expiratory pressure generated by the ventilator, f_R respiratory frequency, *Te* expiratory time, *Ti* inspiratory time, $PEEP_t$ total positive end-expiratory pressure, *Cstat,rs* static compliance of the respiratory system, *Rtot,rs* total resistance of the respiratory system, *τrs,1* dynamic time constant of the respiratory system (slope of the expiratory flow-volume loop), *τrs,2* static time constant of the respiratory system (product of *Rtot,rs* and *Cstat,rs*), $\Delta EELV_1$ direct measurement, $\Delta EELV_2$ mathematical model of Tuxen, $\Delta EELV_3$ mathematical model of Brody, $\Delta EELV_4$ passive inflation method)

	Patients without parenchymal disease ($n = 9$)	Patients with parenchymal disease		
		HMD ($n = 8$)	BPD ($n = 11$)	Bronchiolitis ($n = 6$)
Postnatal age (days) (median, range)	3 (1–8)	3 (2–4)	55 (12–211)	47 (35–65)
Weight (kg) (median, range)	2.7 (1.5–3.5)	2.6 (2.2–3.2)	1.6 (1.2–9)	2.8 (2.3–3.6)
ETT (mm) (median, range)	3 (2.5–3.5)	3.5 (3–3.5)	3 (3–4)	3.3 (3–3.5)
FIO_2 (%)	38 ± 10	65 ± 27	67 ± 25	58 ± 3
PIP (cm H_2O)	20 ± 4	28 ± 4	26 ± 7	32 ± 9
PEEPv (cm H_2O)	0.8 ± 0.8	3.0 ± 0.9	0.8 ± 0.7	1.0 ± 0.9
Vte (ml/kg)	13.8 ± 1.9	9.4 ± 3.1	14.2 ± 4.8	9.9 ± 2.1
f_R (c/min)	38 ± 4	55 ± 7	43 ± 5	39 ± 6
Te (s)	1.03 ± 0.21	0.62 ± 0.14	0.77 ± 0.20	0.97 ± 0.25
Ti (s)	0.59 ± 0.13	0.61 ± 0.13	0.64 ± 0.09	0.61 ± 0.10
PEEPt (cm H_2O)	2.9 ± 0.6	5.0 ± 1.9	4.9 ± 1.7	5.1 ± 1.0
Cstat,rs (ml/cm H_2O per kg)	1.02 ± 0.13	0.44 ± 0.13	0.94 ± 0.16	0.61 ± 0.36
Rtot,rs (cm H_2O/l per s)	57 ± 18	80 ± 24	101 ± 31	114 ± 45
τrs,1 (s)	0.24 ± 0.12	0.12 ± 0.04	0.42 ± 0.23	0.27 ± 0.09
τrs,2 (s)	0.14 ± 0.04#	0.09 ± 0.02	0.30 ± 0.06	0.26 ± 0.03
$\Delta EELV_1$ (ml/kg)	1.6 ± 0.7	1.4 ± 0.9	4.1 ± 1.6**	3.3 ± 1.5*
$\Delta EELV_2$ (ml/kg)	1.3 ± 0.6	1.1 ± 0.8	4.0 ± 1.8**	3.1 ± 1.3*
$\Delta EELV_3$ (ml/kg)	1.6 ± 0.7	2.1 ± 1.1	4.3 ± 1.7*	3.5 ± 1.7
$\Delta EELV_4$ (ml/kg)	1.1 ± 0.5	0.9 ± 0.7	2.7 ± 1.3**	2.4 ± 1.3*

* $p < 0.05$; ** $p < 0.01$ compared to values obtained in infants with HMD; # $p < 0.05$: τrs,1 (s) compared to τrs,1 (s) values)

obtained from the total PEEP values (method 2) and from the Brody's mathematical model (method 3) provided similar results to the direct measurement (method 1). Conversely, graphical extrapolation from the passive expiration method (method 4) underestimated ΔEELV.

These findings are interesting for several reasons. First, few studies have measured the dynamic elevation of FRC or the alveolar pressure at end-expiration in mechanically ventilated neonates or infants. Simbruner [6] found a PEEPi in 19 of the 29 measurements obtained in mechanically ventilated premature newborn infants. PEEPi was also observed in neonates mechanically ventilated at high ventilator frequency [22]. Numerous investigations demonstrated that PEEP increases FRC [23]. Our data provide new evidence that lung volume at end-expiration can be above the relaxation volume in mechanically ventilated infants. Second, we demonstrated that the elevation of FRC can be evaluated accurately from both mathematical extrapolation and total PEEP measurement. Conversely, graphical extrapolation strongly underestimates ΔEELV. This method evaluates the dynamic elevation of FRC and does not take into account the amount of FRC elevation by PEEPv. Inaccuracy of the graphical extrapolation from real breaths of the dynamic elevation of FRC may also explain the discrepancies. Thus, ΔEELV measured by the passive expiration method is lower than actual ΔEELV induced by both PEEPv and PEEPi. However, Tuxen's method requires airway occlusion at both end-inspiration and end-expiration in order to measure PEEPt and respiratory compliance: these gas flow interruptions may not be well tolerated in critically ill patients. As direct measurement of the elevation of FRC requires that the respiratory system is fully relaxed and that the infant does not breathe in until EELV is reached, we suggest using the mathematical extrapolation from the Brody's model to evaluate ΔEELV in mechanically ventilated infants: this method is non-invasive, does not require disruption of gas flow, can be easily performed with all neonatal ventilators, and allows continuous breath-by-breath measurements. However, as for the passive expiration method, mathematical extrapolation from the Brody's model mainly evaluates the dynamic elevation of FRC. The time constant of the respiratory system can be calculated from the slope of the linear expiratory part of the passive flow/volume curve (performed in our study) [16, 19, 24] or directly by fitting an exponential to the passive expiratory volume-time curve.

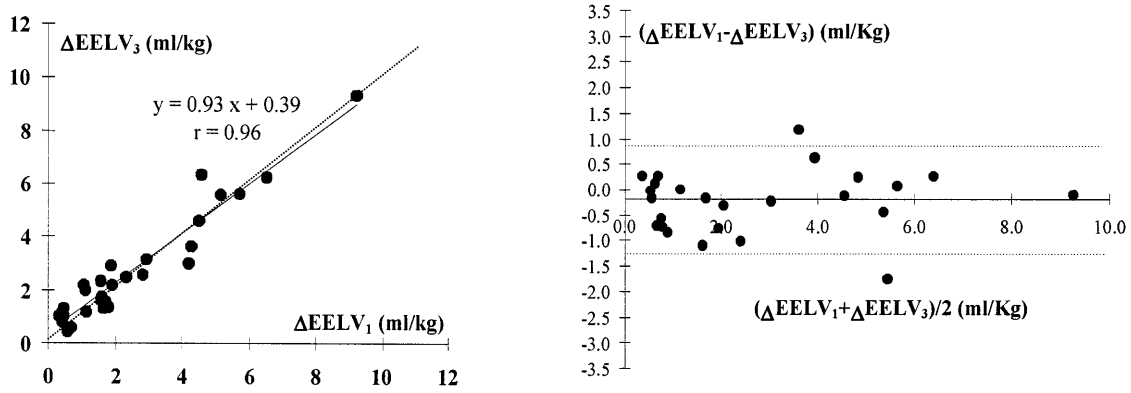
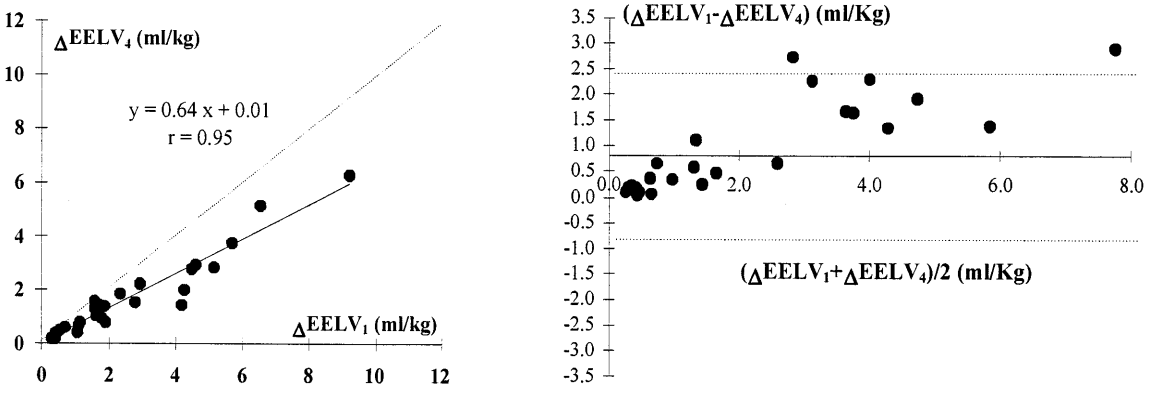


Fig. 5 Comparison between direct measurement and mathematical extrapolation from Brody's model of the volume above EELV at end-expiration by correlation, *dotted line* line of identity, *dashed line* regression line, and Bland and Altman analysis (difference ± 2 SD against mean)

This study has some limitations. First, except for the direct measurement of the elevation of FRC, the three other methods used in this study assume that the respiratory system can be modeled as a single compartment with a single constant compliance and resistance throughout passive expiration (RC model). In infants with airflow limitation, a curvilinear pattern of the expiratory V′/V loop may be observed because of regional lung inhomogeneities and/or because of the mechanical properties of the endotracheal tube. Thus, the basic assumption may not be valid. However, in each infant in this study, the expiratory part of the flow/volume curve was almost perfectly straight. The opposing curvilinearities resulting from lung inhomogeneities and from the presence of the endotracheal tube may explain these results [25]. Bhutani et al. [26] demonstrated that a single RC model was sufficient to describe the mechanical properties of the lung in preterm newborn infants with respiratory failure. Excellent correlation coefficients were obtained by correlating measured values of pressure and flow to those predicted by a first-order linear model [26]. The fact that a good correlation was obtained between direct measurement of ΔEELV and calculation of ΔEELV from PEEPt or mathematical extrapolation from the Brody's model can also be considered as evidence that respiratory mechanics in our infants fit to a linear one-compartment RC model.

Second, several studies demonstrated that end-expiratory alveolar pressure may be, at least in part, determined by the expiratory contraction of abdominal muscles, especially the transverse abdominal muscle [27–30]. Ninane et al. [30], by comparing two groups of spontaneously breathing patients with severe chronic obstructive pulmonary disease (COPD), demonstrated that end-expiratory alveolar pressure was smaller in patients who did not have transverse expiratory activity and suggested that the degree of dynamic pulmonary hyperinflation could be significantly overestimated in patients with COPD [30]. Similar observations were noted by Lessard et al. [28], who studied the relationship

Fig. 6 Comparison between direct measurement and graphical extrapolation from the tidal flow/volume loop (passive expiration method) of the volume above EELV at end-expiration by correlation, *dotted line* line of identity, *dashed line* regression line, and Bland and Altman analysis (difference ± 2 SD against mean)



between end-expiratory alveolar pressure and expiratory swings in gastric pressure in eight tracheally intubated patients and demonstrated that expiratory muscle activity may also increase end-expiratory alveolar pressure without any additional increase in EELV [28]. However, our results do not support the hypothesis that expiratory contraction of abdominal muscles alter total PEEP measurements, as good agreement was found between direct measurements of the elevation of FRC and calculated measurements from total PEEP. Systematic sedation of the infants studied may explain these results.

Third, theoretically, mathematical extrapolation of ΔEELV from the Brody's model (method 3) mainly estimates the dynamic elevation of FRC because the driving pressure of gas flow during passive exhalation is the difference between alveolar pressure and PEEPv: thus, increased FRC induced by PEEPv cannot be measured by this method. We cannot rule out that the good correlation between ΔEELV values obtained from direct measurements (method 1) and from the Brody's model (method 3) in our study may be explained by the low level of PEEPv applied at the airway opening.

Fourth, whereas both direct measurement and calculation of ΔEELV from PEEPt (methods 1 and 2) were performed in static conditions that take into account viscoelastic properties of the respiratory system, both mathematical and graphical extrapolations (methods 3 and 4) were dynamic measurements that are less sensitive to viscoelastic properties of the respiratory system. Especially, they both use time constants calculated from the slope of the flow/volume loop obtained during mechanical ventilation. This dynamic time constant was higher than the static time constant obtained from the occlusion method. These results may explain, at least in part, the discrepancies in the ΔEELV values obtained from direct measurement and from graphical extrapolation.

Fifth, the four proposed methods of measuring ΔEELV in this study require no gas leak around the endotracheal tube, no spontaneous breathing or other muscle activities. Finally, measurements require insertion of a pneumotachograph between the breathing circuit and the endotracheal tube. This equipment increases the dead space. Thus, continuous long-term measurement of ΔEELV may be not recommended in severe respiratory failure in premature infants with severe respiratory failure.

In most of the infants studied, we found that end-expiratory lung volume was above the resting volume. FRC can increase because of applying PEEPv and/or because of incomplete exhalation. Incomplete exhalation can result from a short expiratory or a high expiratory time constant. Thus, dynamic elevation of FRC can be avoided by increasing expiratory time. Hubmayr et al. have demonstrated in normal dogs that the two approaches are not equivalent: for the same overall increase in lung volume, increased ΔEELV from PEEPv is more effective in raising FRC of "fast" lung units with short time constants, whereas increased ΔEELV from PEEPi is more effective in raising the FRC of "slow" units with long time constants [31]. Although some investigators assumed that PEEPt is the sum of PEEPv + PEEPi [3], the evidence does not support this hypothesis. Especially, application of a PEEPv equal to the PEEPi causes the almost complete disappearance of PEEPi in adult patients [32]. To evaluate the relative contribution of incomplete exhalation on ΔEELV, measurements of ΔEELV should be performed at zero end-expiratory pressure. However, a change in mechanical properties of the respiratory system (increase in compliance and in time constant) with a change of PEEP level may alter ΔEELV induced by incomplete exhalation. Thus, the methods used in this study do not allow the determination of the mechanisms of the hyperinflation. However, ΔEELV was higher in infants with a long time constant (bronchopulmonary dysplasia and bronchiolitis). Therefore, we speculate that, in this population of infants, increased ΔEELV was the result of incomplete exhalation.

In summary, mathematical extrapolation from Brody's model is an accurate method for evaluating elevation of FRC in mechanically ventilated infants: it is non-invasive and well tolerated. It can be easily performed with all neonatal ventilators and allows continuous breath-by-breath measurements. However, it must be stressed that it is only the dynamic part of the lung volume elevation that can be estimated by this way. We speculate that this method can be used as a tool to determine the effects of change in ventilator settings (PEEPv, inspiratory time, respiratory rate) on the end-expiratory lung volume and thus to optimize ventilator settings.

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