

Measurement of overinflation by multiple linear regression analysis in patients with acute lung injury

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ABSTRACT: Strategies to optimize alveolar recruitment and prevent lung overinflation are central to ventilatory management of patients with acute lung injury (ALI). The recent description of overinflation using multilinear regression analysis of airway pressure (P_{aw}) and flow (V') data allows a functional assessment of lung mechanics. However, this technique has not been studied in ALI patients.

During 15 positive end-expiratory pressure (PEEP) trials in 10 ALI patients, respiratory elastance was partitioned into volume-independent (E_1) and volume-dependent (E_2V_T) components, where $P_{aw}=(E_1+E_2V_T)V+R_{rs}V'+P_0$; where V is volume, V_T is tidal volume, R_{rs} is respiratory resistance and P_0 is static recoil pressure at end-expiration (equivalent to total PEEP). Then, $\%E_2$ was calculated as $(100E_2V_T)/(E_1+E_2V_T)$; a measure of lung overinflation when $\%E_2>30\%$.

Alveolar recruitment, assessed as a PEEP-induced increase in $V>50$ mL at a constant P_{aw} occurred in 14 of 15 trials (299 ± 34 mL, mean \pm SEM), but was independent of the degree of lung inflation. Lung overinflation was common (six of 15 clinically set PEEP levels) and occurred despite a dynamic elastic distending pressure ($P_{el,dyn}$) <30 cmH₂O during 18 of 36 PEEP titrations. During a PEEP titration the resultant $\%E_2$ was directly related to \dot{y} (peak airway pressure- P_0) ($r_s=0.86$, $p<0.001$) and $\dot{y}(P_{el,dyn}-P_0)$ ($r_s=0.89$, $p<0.001$). The 95% predictive intervals for a 2 cmH₂O change in either driving pressure were $\%E_2$ values of 30.4–68.1% and 32.8–69.2%, respectively.

Single or continuous measurement of $\%E_2$ (a measure of lung inflation) is a readily available method for titrating ventilatory parameters. Further, during a positive end-expiratory pressure titration a change in ventilatory driving pressure ≥ 2 cmH₂O is indicative of overinflation.

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Acute lung injury (ALI) results in an increase in permeability, recruitment of neutrophils and impairment of the surfactant system. Although increased permeability in patients with the acute respiratory distress syndrome (ARDS) is evenly distributed across the lung [1], regional lung inflation is markedly heterogeneous [2, 3]. Increased lung weight tends to collapse a dependent lung, while nondependent lung is more normally aerated. Since a relatively small lung is ventilated, excessive tidal volumes could overdistend some alveoli and produce further lung injury.

In order to prevent overdistension, current recommendations target ventilatory plateau pressures <30 – 35 cmH₂O [4, 5], since total lung capacity is normally achieved at this level of transalveolar pressure. However, the end-inspiratory lung volume (VEI), rather than the airway pressure (P_{aw}), appears to determine whether lung injury occurs [6]. This was confirmed in a recent clinical study where up to 90% of ARDS patients showed evidence of overinflation below a plateau pressure of 35 cmH₂O [7].

Static volume-pressure curve analysis has been used to define lung overinflation, with the upper inflection point denoting a sudden increase in elastance with further inflation. However, static techniques are not widely used. Since a prolonged pause is needed for equilibration of gas flow

and respiratory muscle activity may also result in an unstable end-expiratory lung volume (EELV), the subject must be paralysed. If a super-syringe technique is used allowance must be made for the continuing gas exchange [8] and patients may develop hypoxaemia. Finally, respiratory mechanics are only described at a single point in a continually evolving process.

Dynamic volume-pressure curve analysis offers online, potentially continuous, measurements that do not interfere with ventilation and produce a "functional" description of lung mechanics [9]. Dynamic data may also reflect the contribution of heterogeneous time constants to lung overinflation. At a given respiratory rate short time constant lung units will receive proportionately more ventilation than long time constant lung units, possibly contributing to regional overinflation [10]. This effect would not be detected by static volume-pressure curve analysis, but would contribute to both dynamic curve changes and possibly to ventilator-induced lung injury.

Models for estimating overinflation from dynamic volume-pressure curves, by partitioning dynamic respiratory elastance ($E_{rs,dyn}$) into volume-independent (E_1) and volume-dependent (E_2) components [11–13], have only recently been described. However, this technique has not been

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applied to ventilation strategies of adults with ALI. The purpose of this study was to examine the feasibility of this technique as a direct monitor, and to develop a simple bedside estimate of overinflation during positive end-expiratory pressure (PEEP) trials in this group of patients.

Methods

This study was part of a project examining pulmonary surfactant and surfactant proteins in plasma and was approved by the Committee for Clinical Investigation, Flinders Medical Centre (permit no. 26/93). Informed consent was obtained from the subjects or their closest relative.

Study design

Ten ALI patients, eight with ARDS and two at risk, were studied (total of 15 PEEP trials, table 1). Multiple studies on separate days were conducted on patients numbers 8, 9 and 10. On each occasion their results were used to adjust the subsequent ventilator settings. All patients were sedated with an infusion of morphine and midazolam and were paralysed with pancuronium bromide. Their Acute Physiology and Chronic Health Evaluation (APACHE II) score and predicted mortality during the first 24 h in the intensive care unit (ICU) [15], and their lung injury score [14] at the time of study were calculated. Patients were ventilated using a Puritan-Bennett 7200ae ventilator (Puritan-Bennett Corp., Carlsbad, CA, USA) with a tidal volume (V_T) of 8–10 mL·kg⁻¹, a square-wave inspiratory flow (V') pattern and an inspiratory:expiratory ratio (I:E) exceeding 1:1. PEEP trials were initially performed at the current, clinically set level of PEEP (baseline) and then repeated at 30 min intervals following random PEEP changes (5–15 cmH₂O) with the V' , V_T and I:E ratio kept constant. Arterial blood was collected for the calculation of the ratio of arterial oxygen tension (P_{a,O_2})/inspiratory oxygen fraction (F_{I,O_2}) immediately before the initial PEEP study. This was

taken as representative of the baseline lung function. The plasma and pulmonary surfactant data are reported elsewhere [16].

Equipment and procedure

Flow was measured with a heated, Fleisch-type pneumotachograph (HP-47034A, Hewlett-Packard, Palo Alto, CA, USA) and transducer (21072A; Hewlett-Packard), which had been calibrated over the range 0–300 L·min⁻¹ with a flow calibration set (18987-1; Gould Godard VB, Biltoven, The Netherlands). The pneumotachograph was connected between the Y-piece of the ventilator tubing and the endotracheal tube. P_{aw} was measured proximal to the endotracheal tube by a precalibrated (water manometer) strain gauge transducer (Bell and Howell 4-327-I; Trans-America Delaval, Pasadena, CA, USA). Flow and P_{aw} were recorded on a personal computer via a 12-bit analogue-to-digital converter (DT2801; Data Translation, Marlboro, MA, USA) at 100 Hz for later data analysis (ANADAT 5.1; RHT-InfoDAT, Montreal, Canada).

After 30 min at each PEEP level, 60 s of data were collected, the last 20 s of which were used to measure the increase in EELV ($\dot{y}EELV$) caused by the total PEEP ($PEEP_{tot}$); where this equals extrinsic PEEP ($PEEP_e$) plus any intrinsic PEEP ($PEEP_i$) present. In brief, the ventilator frequency was set at zero and the $PEEP_e$ removed, allowing the respiratory system sufficient time to reach its relaxation volume (V_r) [17]. Volume (V) was obtained from the tidal breath data, by digital integration of the V' signal and referenced to V_r by adding $\dot{y}EELV$. The signals were then breath-averaged and the dynamic volume-pressure relation was obtained by plotting V against P_{aw} . The PEEP-recruited lung volume was measured as the increase in volume at a constant P_{aw} , typically 20 cmH₂O (fig. 1), with an increase in volume >50 mL considered to be evidence of lung recruitment, as described by RANIERI *et al.* [17, 18]. VEI was calculated as $\dot{y}EELV + V_T$.

Table 1. – Characteristics of the study patients

Age yrs	Sex	Day of MV	ETT size	Cause of ALI	PEEP	$P_{a,O_2}/F_{I,O_2}$	% E_2 *	$P_{el,dyn}$	LIS ⁺	APACHE II/PM [‡]	Outcome
74	M	3	9.0	Ruptured AAA	5	176	3.7	26.6	1.5	18/0.17	S
24	M	3	9.0	Lung contusion	10	228	38.5	30.4	2.25	17/0.09	S
72	F	1	8.0	Legionnaire's disease	7	66	49.6	28.9	2.75	41/0.93	D
48	M	3	9.0	Pancreatitis	5	245	-2.2	22.5	1.5	21/0.51	S
68	F	4	7.0	Pulmonary embolus	7.5	145	16.6	20.2	1.75	27/0.57	S
54	M	2	9.0	Aspiration	7.5	129	27.7	25.5	2.67	26/0.57	S
73	M	7	9.0	Aspiration	10	102	46.5	29.8	3.3	27/0.68	D
72	M	1	9.0	Pneumonia	8.5	140	24.3	30.3	2.75	28/0.67	D
		3			10	116	40.9	33.1	3		
81	M	1	9.0	Aspiration	4	82	40.5	19.0	2.25	25/0.50	S
		2			7.5	112	50.5	22.8	2.75		
		7			7.5	121	31.2	17.7	2.5		
47	M	1	9.0	Liver transplant	10	157	12.1	23.0	2.75	31/0.60	S
		3			7.5	180	31.0	22.8	2		
		5			10	162	32.4	27.6	2.5		

MV: mechanical ventilation; ETT: endotracheal tube; ALI: acute lung injury; PEEP: positive end-expiratory pressure; P_{a,O_2} : arterial oxygen tension; F_{I,O_2} : inspiratory oxygen fraction; % E_2 : degree of inflation; $P_{el,dyn}$: dynamic elastic airway pressure; LIS: lung injury score; APACHE II: Acute Physiology and Chronic Health Evaluation II score; PM: predicted mortality; M: male; F: female; AAA: abdominal aortic aneurysm; S: survived; D: died. *: % E_2 equals $100 E_2 V_T / (E_1 + E_2 V_T)$ where V_T is tidal volume and E_1 and E_2 are derived from the volume-dependent single compartment model [11]; +: lung injury scores [14]; ‡: predicted mortality was calculated from published data [15] and APACHE II scores from first 24 h of intensive care unit admission.

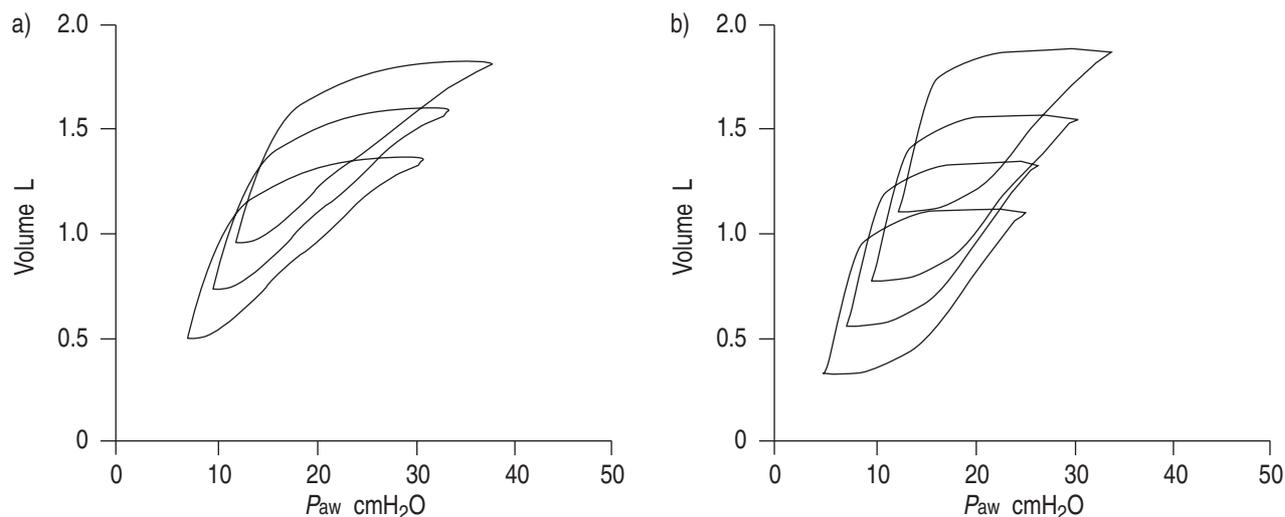


Fig. 1. – Typical breath-averaged dynamic volume-pressure curves, referenced to the relaxation volume of the respiratory system, from two patients studied. a) In patient number 7 positive end-expiratory pressure (PEEP) incrementally recruited lung volume, as detected by an upward displacement of the curve at a constant airway pressure (P_{aw}), typically 20 cmH_2O . The initial degree of inflation ($\%E_2$) of 41.8%, suggests that overinflation was already present. With each PEEP step the $\%E_2$ monotonically increased to 46.5% and then to 51.1%. b) Similar data are presented for patient number 5 and although the $\%E_2$ progressively increased from 8.7% to 28.1% the lung was never overdistended. Recruitment did not occur between the second and third PEEP titration; however, upward displacement of the volume-pressure curve at the fourth level of PEEP indicates further lung recruitment.

Data analysis

Multilinear regression analysis of the entire (inspiratory and expiratory) P_{aw} , V and V' data was performed using: 1) a linear single-compartment model (LSCM) where $P_{aw} = E_{rs,dyn}V + R_{rs}V' + P_o$, and 2) a volume-dependent single-compartment model (VDSCM) where $P_{aw} = (E_1 + E_2V)V + R_{rs}V' + P_o$, where R_{rs} is the dynamic respiratory system resistance and P_o is the static recoil pressure at end-expiration which is equivalent to PEEP_{tot} [11]. Consequently, when using the VDSCM, $E_{rs,dyn} = (E_1 + E_2VT)$. PEEP_i was calculated as the difference between P_o and the minimum P_{aw} [11, 19, 20] and was minimal in all patients ($0.24 \pm 0.00 \text{ cmH}_2\text{O}$). The $\%E_2$ was calculated as $(100E_2VT)/(E_1 + E_2VT)$ [11], and $P_{el,dyn}$ calculated as $(E_1 + E_2VT)VT + P_o$. Since $P_{el,dyn}$ is equivalent to peak pressure (P_{peak}) minus the resistive pressure this can be considered as the alveolar distending pressure, often measured clinically as the plateau pressure.

Results are expressed as means \pm SEM. Since there was no reason to assume that a linear relationship held between the variables, the associations were tested with Spearman rank order correlations (r_s) and the fit (r^2) of the LSCM and VDSCM models was compared using a Wilcoxon signed rank test. From each PEEP titration the values for $\hat{y}P_{el,dyn} - P_o$ and $\hat{y}P_{peak} - P_o$ with the resultant $\%E_2$ were recorded, the intercept tested with linear regression analysis, and 95% predictive intervals for $\%E_2$ values following a 2 cmH_2O change calculated. Finally, the initial PEEP trial data ($n=10$) and those with repeated trials in three patients ($n=15$) were both analysed.

Results

Although both models fitted the data well, with r^2 generally exceeding 0.98, the VDSCM described the overinflated data more accurately than did the LSCM ($p < 0.001$) (fig. 2). Consequently, only the VDSCM data are presented.

Multilinear regression analysis and lung overinflation

Over the range of PEEP studied, the $E_{rs,dyn}$ increased ($2.4 \text{ cmH}_2\text{O} \cdot \text{L}^{-1}$, 95% confidence interval (CI) 0.4–4.4 $\text{cmH}_2\text{O} \cdot \text{L}^{-1}$) owing to the combined effects of a fall in E_1 ($-2.7 \text{ cmH}_2\text{O} \cdot \text{L}^{-1}$, 95% CI -1.1 – $-4.3 \text{ cmH}_2\text{O} \cdot \text{L}^{-1}$) and a rise in E_2VT ($5.1 \text{ cmH}_2\text{O} \cdot \text{L}^{-1}$, 95% CI 3.1–7.1 $\text{cmH}_2\text{O} \cdot \text{L}^{-1}$). Consequently, the $\%E_2$ rose (17.2%, 95% CI 11.3–23.0%). The change in E_1 correlated directly with the initial $\%E_2$ ($r_s = 0.59$, $p = 0.02$) and inversely with the $\hat{y}\%E_2$ ($r_s = -0.60$, $p = 0.02$).

Overinflation, as judged by a $\%E_2 > 30\%$, was common and correlated with VEI ($r_s = 0.70$, $p < 0.001$, $r_s = 0.80$, $p < 0.001$ for 10 PEEP trials; fig. 3) and indirectly with the $P_{a,O_2}/F_{I,O_2}$ ratio ($r_s = -0.79$, $p < 0.001$, $r_s = -0.87$, $p < 0.001$ for 10

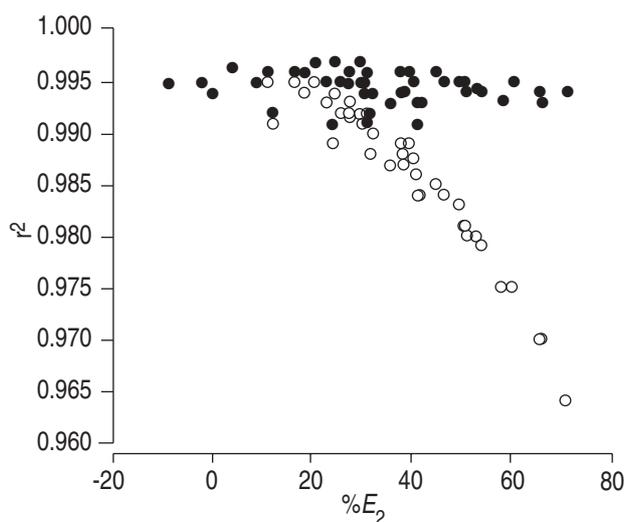


Fig. 2. – The r^2 data for the volume-dependent, single-compartment model (VDSCM; ●) were unaffected by the degree of inflation ($\%E_2$), whereas the model fit of the linear single-compartment model (LSCM; ○) deteriorated with progressive lung inflation.

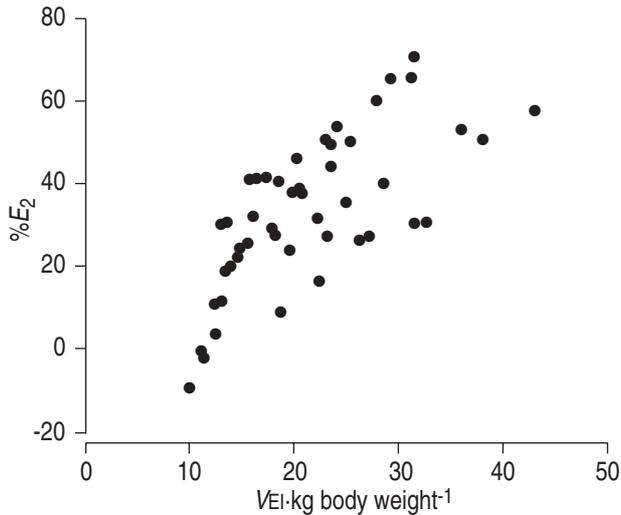


Fig. 3. – On examination of all positive end-expiratory pressure titrations (n=49) the degree of lung inflation (% E_2) was directly related to the end-inspiratory volume per kilogram body weight above the resting lung volume ($VEI \cdot kg^{-1}$) ($r_s=0.70$, $p<0.001$). When only 10 PEEP trials (n=35 PEEP titrations) were tested a similar relationship was found, Spearman rank correlation coefficient ($r_s=0.80$, $p<0.001$).

PEEP trials). During a PEEP titration the resultant % E_2 was highly correlated with the change in ventilatory driving pressures, $\hat{y}(P_{el,dyn}-P_o)$ and $\hat{y}(P_{pk}-P_o)$ ($r_s=0.89$, $p<0.001$ and 0.86 , $p<0.001$, respectively; $r_s=0.92$, $p<0.001$ and 0.90 , $p<0.001$, respectively, for 10 PEEP trials; fig. 4), with intercepts of $30.7 \pm 1.6\%$ and $32.1 \pm 1.6\%$ (linear regression analysis). The 95% predictive intervals for % E_2 values following a 2 cmH₂O change in ventilatory driving pressure were 32.8–69.1% and 30.4–68.1%, respectively (linear regression analysis). While a high $P_{el,dyn}$ predicted overinflation, ventilation titrated to a low $P_{el,dyn}$ would not have prevented overinflation, with 50% of patients with a $P_{el,dyn} \delta 30$ cmH₂O having a % $E_2 > 30\%$ and 53% of patients with a $P_{el,dyn} \delta 35$ cmH₂O having a % $E_2 > 30\%$ (table 2, fig. 5).

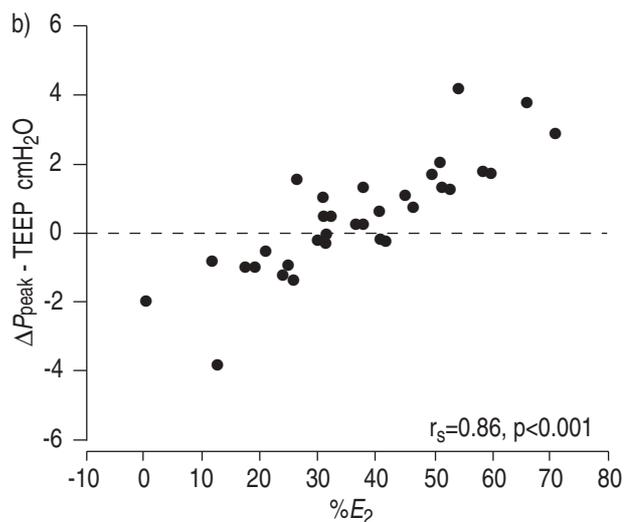
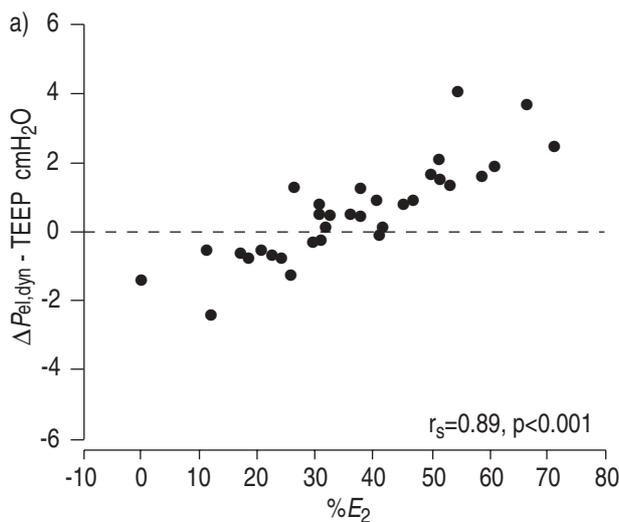


Fig. 4. – The change in the dynamic elastic airway pressure minus total end-expiratory pressure ($\hat{y}P_{el,dyn} - TEEP$) and b) the change in peak airway pressure minus TEEP ($\hat{y}P_{peak} - TEEP$) correlated with the degree of lung inflation (% E_2), with intercepts (0 cmH₂O) of 30.7% and 32%, respectively (linear regression analysis). When only 10 positive end-expiratory pressure (PEEP) trials (n=35 PEEP titrations) were tested almost identical results were found, with rank correlation coefficients ($r_s=0.92$, $p<0.001$ and $r_s=0.90$, $p<0.001$ for the relationship between $\hat{y}P_{el,dyn} - TEEP$ or $\hat{y}P_{peak} - TEEP$ and % E_2 respectively).

Table 2. – Respiratory parameters from 49 positive end-expiratory pressure titrations

	n	$P_{el,dyn} \delta 30$	$P_{el,dyn} > 30$	$P_{el,dyn} \delta 35$	$P_{el,dyn} > 35$
% $E_2 < 30$	20	18	2	20	0
% $E_2 > 30$	29	18	11	23	6
n		36	13	43	6

% E_2 : degree of inflation ($100E_2VT/(E_1+E_2VT)$, where VT is tidal volume and E_1 and E_2 are derived from the volume-dependent single compartment model [11]. A % $E_2 > 30\%$ indicates overinflation. $P_{el,dyn}$: dynamic elastic airway pressure.

Alveolar recruitment

Across the range of applied PEEP, 14 of the 15 PEEP trials showed lung recruitment in excess of 50 mL (299 ± 34 mL). Six PEEP trials had a baseline % $E_2 > 30\%$; however, there was no relationship between % E_2 and the recruited volume ($r_s=0.22$), with the non-overinflated patients recruiting a similar volume (311 ± 50 mL) to the overinflated patients (234 ± 50 mL, $p=0.48$). A weak correlation was found between the recruited volume and $\hat{y}\%E_2$ ($r_s=0.62$, $p=0.014$), but no relation was found between the recruited volume and $\hat{y}E_1$ ($r_s=-0.41$).

Discussion

Addition of a volume-dependent elastance term to multilinear regression analysis improves the model fit in mechanically ventilated patients with ALI. Overinflation was common in the study patients and not well predicted by the alveolar distending pressure; however, changes in ventilatory driving pressure during PEEP titrations were highly correlated with overinflation and could provide a simple, immediately available bedside estimate. Since these data are modelled from dynamic volume-pressure data, this technique could be modified to monitor overinflation continuously and, potentially, to assist in a servo-controlled mode of ventilation.

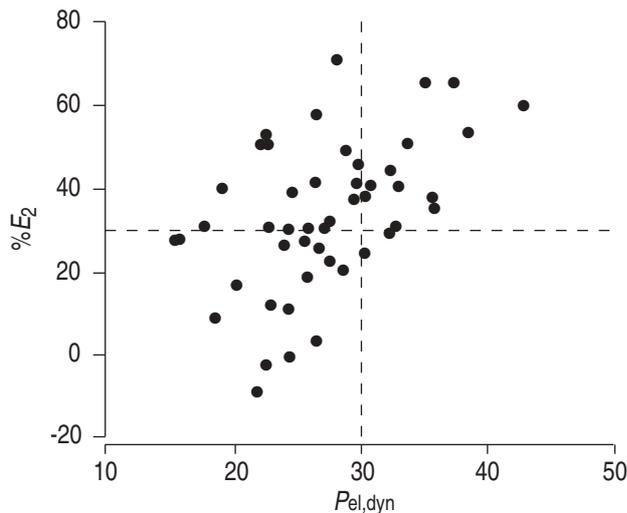


Fig. 5. – Although a broad correlation was found between the degree of lung inflation ($\%E_2$) and the dynamic elastic airway pressure ($P_{el,dyn}$), 50% of the data with a $P_{el,dyn} < 30$ cmH₂O were overinflated ($\%E_2$ (rank correlation coefficient (r_s)=0.47, $p=0.0007$) $> 30\%$). When only 10 positive end-expiratory pressure (PEEP) trials ($n=35$ PEEP titrations) were tested almost identical results were found ($r_s=0.59$, $p<0.001$).

Critique of methodology

Although ROUSSELOT *et al.* [12] and PESLIN *et al.* [13] found little improvement in model fit with the addition of a volume-dependent elastance term, it is probable their patients were not overinflated. The present data comparing the linear and volume-dependent models are almost identical to those of KANO *et al.* [11], who purposefully induced overinflation in anaesthetized dogs. While both models showed high r^2 values, the r^2 for the LSCM became less robust as $\%E_2$ increased (fig. 2). Consequently, we have only reported data from the VDSCM.

Fitting the data to the VDSCM means that $E_{rs,dyn} = E_1 + E_2V$; in other words $E_{rs,dyn}$ increases linearly with volume, with a slope of E_2 ; however, these values will only be applicable to the data set fitted. Increasing PEEP generally resulted in a recruitment of lung units, leading to a fundamental change in the respiratory system being ventilated. This was reflected by altered values for E_1 and E_2V , with the fall in E_1 consistent with a greater mass of lung being ventilated and the increase in E_2V reflecting overdistension of inflated alveoli. If the respiratory system were unchanged by changing PEEP, E_1 and E_2V should remain constant. While this does not mean that the true volume-pressure is exactly a quadratic function, the great utility of the VDSCM is that it is a better model of the respiratory system in ALI patients than a LSCM that also yields rapid, sensible and robust information from routinely available measurements.

Since flow and resistance are part of the multilinear regression model, measures of elastance are relatively independent of ventilatory flow pattern or resistance. KANO *et al.* [11] also demonstrated that endotracheal tube size and resistance did not influence $\%E_2$; consequently, no account was taken of this in the present study. However, visual assessment of volume-pressure relations and the ratio of the final 20% of inspiratory dynamic compliance to the total dynamic compliance are influenced by flow-resistive effects [11] and may not easily be interpreted.

For example, in figure 1a the degree of lung overinflation and its increase during incremental PEEP is not obvious until the $\%E_2$ is calculated. While analysis of a constant inspiratory flow pattern [18] minimizes resistive effects and is conceptually similar to the current model, it precludes analysis of many clinically used flow or pressure patterns. Consequently, the VDSCM modification of the equation of motion offers a number of important advantages.

Respiratory system elastance is the sum of lung and chest wall elastance, both of which may be increased in patients with ALI. Since no oesophageal balloon was inserted in the present study patients these components cannot be separated out. However, while chest wall elastance is commonly increased in ALI [21], ROUPIE *et al.* [7] found that overinflation determined from static respiratory system volume-pressure curves reflected lung overinflation since the chest wall component remained linear. Consequently, overdistension measured using volume-dependent elastance should reflect lung overinflation. Indeed, while a number of patients may have had distinct increases in chest wall elastance due to abdominal distension (patients numbers 1, 4 and 10, day 1), their $\%E_2$ still correlated with VEI as expected. Consistent with the notion that in these patients abdominal distension may have increased $E_{rs,dyn}$, it is noteworthy that all three had lower $\%E_2$ values despite alveolar distending pressures similar to the other patients studied. Finally, negative $\%E_2$ values were present in all three patients at a PEEP_e of 5 cmH₂O, suggestive of atelectasis and a negative volume dependence [9].

Assessment of overinflation

Based on direct comparison with static volume-pressure curves, KANO *et al.* [11] proposed that $\%E_2 > 30\%$ indicated overinflation. In the absence of static volume-pressure curves in the present study, the relationship between $\%E_2$ and the VEI·kg body weight⁻¹ was examined. Pooling all data, $\%E_2$ correlated strongly with VEI·kg body weight⁻¹ and when each PEEP trial was plotted individually against VEI·kg body weight⁻¹, $\%E_2$ increased monotonically. This is consistent with $\%E_2$ reflecting progressive inflation, while the intercept of the $\%E_2$ versus change in ventilatory driving pressure is consistent with the notion of a $\%E_2 > 30\%$ representing overinflation. Finally, TUXEN *et al.* [22] proposed a safe VEI·kg body weight⁻¹ in asthmatic patients was < 20 mL·kg⁻¹, very close to the intercept of VEI·kg body weight⁻¹ with a $\%E_2$ of 30% in the present study.

ROUPIE *et al.* [7] found that ARDS patients had an upper inflection point (24 ± 1 cmH₂O, range 18–37 cmH₂O) on their static volume-pressure curve. Their plateau pressure commonly exceeded the upper inflection point (80% incidence) when a VT of 10 mL·kg⁻¹ was used; however, this decreased dramatically (0–20% incidence) with VT of 5.5–7 mL·kg⁻¹. Using impedance plethysmography, BRUNET *et al.* [23, 24] also found an upper inflection point in ARDS patients, albeit at generally higher pressures than ROUPIE *et al.* [7]. However, almost half the time this occurred at $P_{aw} < 30$ cmH₂O. In agreement with these studies, overinflation was common in the present study (fig. 5, table 2) despite attempts to limit the alveolar distending pressure. These data suggest that maintenance of a P_{aw} below an arbitrary limit poorly limits the incidence of overdistension.

Since the consequences of lung overdistension include ALI and overt barotrauma, it is likely to be important that overdistension be monitored directly and mechanical ventilation titrated accordingly; this was a major impetus for the current study. However, since derivation of $\%E_2$ from a dynamic volume-pressure curve requires a number of mathematical steps, it currently remains a research tool. Potentially, these steps can be programmed into modern ventilators with $\%E_2$ continuously displayed and used to adjust ventilator settings.

The change in ventilatory driving pressure was also examined as a measure of $\%E_2$ since equivalent pressure data (plateau pressure or, more correctly, the pressure immediately after end-inspiratory occlusion for $P_{el,dyn}$ [25] and $PEEP_{tot}$ for P_0) are currently available at the bedside. The strong correlation of the change in ventilatory driving pressure with $\%E_2$ following a change in the applied PEEP (fig. 4) offers an indirect measure of overinflation that could be used independently of the volume-pressure curve, with a rise in driving pressure $\dot{S}2$ cmH₂O indicative of overinflation. Intuitively, this makes sense, as these pressure changes will only increase when there is an increase in E_{rs} and this will reflect an increase in $E_2 V_T$.

Alveolar recruitment and overdistension

Concurrent with PEEP-induced recruitment, E_1 fell, probably reflecting a greater mass of ventilated lung, and $\%E_2$ rose; however, neither was related to the volume recruited. Consistent with computed tomography scan data showing PEEP-induced recruitment of collapsed lung with concurrent overinflation of aerated lung [26], recruitment was found to be independent of overinflation and $\dot{y}E_1$ was inversely related to $\dot{y}E_2$. As incremental PEEP resulted in increases in $VEI \cdot kg$ body weight⁻¹, and a monotonic increase in $\%E_2$, overinflation often accompanied recruitment. Perhaps use of lower V_T than used in the current study (8–10 mL·kg⁻¹) would have allowed recruitment without overinflation. Indeed, AMATO *et al.* [27] reported an improvement in lung function using a V_T of 6 mL·kg⁻¹ and a PEEP level determined from a static volume-pressure curve, compared to a randomized control group undergoing conventional ventilation.

The volume-dependent model was used to examine theoretically the relative value of V_T reduction as a strategy to prevent overinflation. Assuming that E_2 is unchanged by decreasing V_T , compare the two situations: 1) where $E_1 = 2E_2 V_T$ with $\%E_2$ of 33%, and 2) where $E_1 = E_2 V_T$ with $\%E_2$ of 50%. In the first instance a reduction in V_T to two-thirds of its initial value would reduce $\%E_2$ by one-quarter to a $\%E_2$ of 25%, but a reduction of only 20% to a $\%E_2$ of 40% would occur in the second instance. Hence, the higher the ratio of $E_2 V_T : E_1$, the greater the degree of overinflation, with a concomitant reduction in the effectiveness of V_T reduction in reducing $\%E_2$. Using this strategy, ROUPIE *et al.* [7] reported that a V_T reduction of one-third resulted in fewer than 10% of their patients exceeding the upper inflection point, with a rise in the arterial carbon dioxide tension (P_{a,CO_2}) from 5.9 to 10.2 kPa (44 to 77 mmHg). It follows from the present data that their $E_2 V_T : E_1$ ratio would lie between the two examples discussed above.

In contrast to patients with ARDS, ROUPIE *et al.* [7] found that patients with mild ALI rarely demonstrated an upper inflection point (maximum VEI examined 1,600 mL), suggesting that overinflation during conventional techniques of mechanical ventilation reflects the severity of the underlying lung injury and heterogeneity of the respiratory mechanics. Consistent with this, in the present study the $P_{a,O_2} / F_{I,O_2}$ ratio was found to be inversely related to $\%E_2$.

Conclusions

This study described the use of a volume-dependent, single-compartment model to estimate overinflation in patients with ALI. Overinflation was common, and paradoxically not prevented by avoidance of an elastic distending pressure in excess of 30 cmH₂O. If surfactant comprises two-thirds of lung elastance [28], this could be explained by impaired surfactant function, with a decrease in surface tension hysteresis [29] and a failure to increase pressure in overinflated alveoli.

Overinflation may be readily estimated as an increased ventilatory driving pressure, the difference between positive end-expiratory pressure and either the peak or static airway pressure, $\dot{S}2$ cmH₂O during a positive end-expiratory pressure titration. However, the volume-dependent, single-compartment model analysis could be continuously displayed with positive end-expiratory pressure and tidal volume adjusted automatically in order to minimize ventilator-induced lung injury. Prospective studies are needed to determine whether this approach to reducing ventilator-induced lung injury results in improved outcome.

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