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The upper inflection point of the pressure-volume curve

Influence of methodology and of different modes of ventilation

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Abstract *Objective:* The pressure-volume (P/V) curve has been proposed as a tool to adjust the ventilatory settings in cases of acute respiratory distress syndrome (ARDS). The aim of this study was to test the influence of P/V tracing methodology on the presence and value of the upper inflection point (UIP). *Methods:* In 13 medical ARDS patients, the interruption and the automated low flow inflation methods were compared while the patients were ventilated at conventional (10–12 ml/kg) and at low (5–6 ml/kg) tidal volume (Vt). Two levels of inspiratory flow and insufflation time were used (3 and 6 s). *Results:* No significant difference in UIP was found between the static and the dynamic methods, whatever the flow used. At Vt 10–12 ml/kg, the static and dynamic UIPs were 22.4± 4.4 cmH_2O and 22.1±4.5 cmH_2O (p=0.86), respectively; at Vt of 5–6 ml/kg, the static and dynamic UIPs were 26.6±4.1 cmH_2O and 25.5±5 cmH_2O (p=0.34), respectively. Significant differences in UIP were found, in the static and dynamic conditions, between the two levels of Vt (p<0.005): it was lower with the higher Vt, suggesting that UIP is dependent on previous tidal alveolar recruitment. *Conclusion:* Interruption and continuous flow techniques gave similar results, but the previous Vt influences the pressure value of the UIP.

Keywords Acute respiratory distress syndrome (ARDS) · Mechanical ventilation · Recruitment

Introduction

The pressure-volume (P/V) curve of the respiratory system is used to describe the mechanical characteristics of the lungs in acute respiratory distress syndrome (ARDS) [1, 2, 3, 4] and it has been proposed as a guide with which to modify the ventilatory settings at bedside, with the goal of limiting lung damage related to mechanical ventilation [5, 6, 7, 8, 9, 10, 11].

Several parameters can be identified to adjust ventilatory settings. The shape of the P/V curve is described, in ARDS, as having three main segments. A non-linear lower segment characterized by a low compliance is separated by a lower inflection point (LIP) from a linear intermediate segment with a higher compliance and terminated by an upper non-linear segment over which compliance tends to fall with increasing volume [1, 3, 4, 12] These latter two segments are separated by an upper inflection point (UIP). In classic respiratory physiology, the upper segment reaches total lung capacity and alveolar over-distension probably takes place since a slight increment in volume is accompanied by a major increase in airway pressure.

Few studies have investigated the UIP and a full understanding of the nature, the significance and the validity of the UIP is still lacking. In patients with ARDS, Roupie et al. [6] showed that, by using "conventional" tidal volume (Vt) around 10 ml/kg of body weight, end-inspiratory plateau pressure surpassed the UIP in 85% of patients, suggesting that they were at risk of over-distension and baro-

trauma. Based on these mechanical properties of diseased lungs, a concept of "protective lung strategy" using the P/V curve to adjust positive end-expiratory pressure (PEEP) has been successfully implemented by Amato et al. [8, 10]. More recently, Ranieri, using a similar approach to adjust both PEEP and Vt, showed that the protective approach produced less inflammatory mediators than a more aggressive ventilator mode [13].

Ranieri et al, in a series of ARDS cases using different methodology, failed to document UIP in five among eight patients [14]. He showed later that the presence of UIP was evidenced only when patients were ventilated with low Vt (5–6 ml/kg) and/or with no PEEP. Mergoni et al. [15] reported very low levels of UIP in a series of 13 cases of ARDS. Servillo et al. [9] had earlier demonstrated the influence of the methodology used for tracing P/V curves on the compliance of the upper segment above UIP. Finally, Hickling [16] and Jonson [17] questioned the significance of the UIP, from the analysis of mathematical models of P/V curves, and suggested that UIP corresponded to the end of alveolar recruitment instead of over-distension.

The purpose of the present study was to assess the influence of methodology and the previous mode of mechanical ventilation (tidal volume) on the presence and on the level of the UIP in patients with ARDS. The interruption and a slow continuous inflation technique were compared and the role of different modes of ventilation was assessed by using two different Vts to ventilate the patients.

Materials and methods

Patients

The study was performed in the intensive care unit of the University of Naples "Federico II" after local ethics committee approval. Informed consent was obtained from patients' next of kin.

During a 8month period, all medical patients requiring mechanical ventilation for more than 24 h with an inspiratory fraction of oxygen (FIO_2) equal to or greater than 0.5 were considered as potential candidates. Exclusion criteria were a documented history of COPD, the presence of a chest tube with persistent leak or contraindication for sedation and paralysis and any cause of chest wall abnormalities (recent abdominal surgery, ascites, pleural effusion, edema of the thorax). Adult medical patients suffering from ARDS (LIS >2.5) were considered eligible [18, 19]. Patients were intubated with a cuffed endotracheal tube (7.5–8.5 mm inner diameter) and ventilated in volume-controlled mode at constant inspiratory flow with a Servo 900 C Ventilator (Siemens-Elema, Sweden). The basal ventilation was chosen by the attending physicians. Tidal volume was 8–10 ml/kg of actual body weight (BW), respiratory rate (RR) 14–18 breaths/min and inspiratory and post-inspiratory pause time 33 and 5% of the respiratory cycle, respectively. The PEEP level was chosen to maintain adequate oxygenation. Except for changes in Vt, the ventilatory settings were kept constant throughout the experiment. Patients had been mechanically ventilated for a period of 1–3 days prior to the present investigation and had been clinically stable during the preceding 6–8 h. Patients were monitored as clinically required. All patients were sedated and paralyzed by a continuous infusion of propofol (6–10 mg/kg per h) and pancuronium bromide (0.1–0.2 mg/kg) and studied in the supine position. A physician not involved in the experimental procedure was always present to provide patient care. The general characteristics of the ARDS patients are reported in Table 1.

Equipment

The Servo Ventilator was connected to an IBM-compatible personal computer through a ventilator/computer interface, as previously described [9] (Fig. 1). The computer emitted analog signals which, transmitted via the external control socket of the ventilator, allowed the computer to take over control of RR, PEEP and minute ventilation. P/V curves were recorded using the flow and expiratory pressure transducers of the ventilator. These were daily calibrated against a water manometer and a 1l syringe. Flow and volume were calibrated to yield data at body temperature and pressure, saturated with water vapor, i.e. BTPS. The signals of pressure and flow were fed to the computer and analog-to-digital (A/D) converted at 50 Hz. Flow rate was corrected for gas compression in the tubing. Volume was then calculated by integration

Table 1 General characteristics of the patients (*SAPS* simplified acute physiology score [20], *LIS* lung injury score [19], *PEEP* positive end-expiratory pressure, PaO_2/FIO_2 ratio between arterial oxygen tension and inspired oxygen tension)

Patients No.	Age (year)	Sex	Weight (kg)	LIS	SAPS	PEEP (cmH_2O)	PaO_2/FIO_2 (PEEP)	Diagnosis	Outcome
1	63	F	80	2.75	14	10	164	Pneumonia	Alive
2	70	M	50	3.25	17	12	130	Lymphoma	Dead
3	71	F	60	3	11	12	143	Sepsis syndrome	Dead
4	73	F	85	3	17	10	116	Pneumonia	Dead
5	45	F	90	2.75	12	10	164	Pneumonia	Alive
6	73	F	95	3.25	14	10	96	Lymphoma	Dead
7	25	M	70	2.75	16	14	200	Sepsis syndrome	Dead
8	38	M	80	3	14	10	146	Pneumonia	Alive
9	57	M	90	3.25	20	8	180	Myocardial infarction	Dead
10	60	F	85	2.75	17	10	175	Sepsis syndrome	Dead
11	58	M	50	3	20	12	140	Pneumonia	Dead
12	61	M	80	2.75	14	8	180	Lymphoma	Alive
13	28	F	65	3	17	10	160	Pneumonia	Dead
Mean	55.5		75	3	15.6	10.4	153.3		
± SD	16.5		14	0.2	2.7	1.6	28.7		

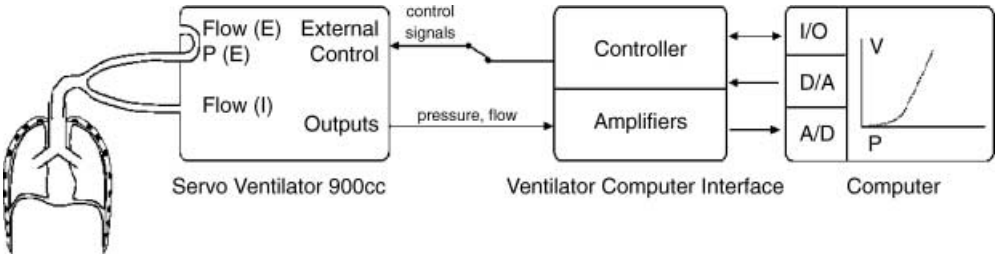

Fig. 1 The ventilator was computer controlled via an interface to yield appropriate breathing patterns for automated determination of static and elastic pressure-volume curves. The Servo Ventilator 900C is equipped with a socket for electronic signals allowing external control of ventilator function. The personal computer was provided with analog-to-digital (A/D) and digital-to-analog (D/A) converters and a digital interface to allow control of the ventilator and recording of airway pressure and airway flow

of flow. During the procedure the computer continuously recorded pressure and flow and these data were automatically transferred to a spreadsheet (EXCEL 5.0, Microsoft) prepared for automatic analysis.

Dynamic pressure-volume curves

Dynamic P/V curves (P_{dyn}/V) were recorded during one single insufflation at constant flow. After a normal complete inspiration, the following expiration was prolonged to 6 s to allow for complete flow cessation. When patients had previously been ventilated with PEEP, the computer forced the ventilator to ZEEP during a prolonged expiration and the study breath inspiration started from ZEEP. The duration of the following inspiratory phase (insufflation) was 6 s or 3 s. The computer controlled the flow rate during the insufflation so that the volume reached 25 ml/kg body weight during these 3 or 6 s. This insufflated volume was chosen to result in a peak pressure of about 45 cmH_2O. The insufflation was automatically interrupted at a pressure of 50 cmH_2O. During a prolonged expiration following the insufflation, lung volume was allowed to return to the previous level of the end-expiratory pressure.

In order to obtain the dynamic elastic recoil pressure in the distal airways and the alveoli, the resistive pressure drop in the tubing and the large airways during the insufflation was subtracted from the pressure measured. This resistive pressure drop was calculated from the tube resistance measured in vitro and the resistance of the airways measured from a preceding, unperturbed breath, according to Varène and Jacquemin [20], as previously described [9].

In order to make unbiased statistical comparisons between conditions and patients, the main part of the P_{dyn}/V curve was defined mathematically. Each curve was analyzed as comprising three segments, separated by a lower and an upper inflection point (LIP and UIP, respectively), and the segment between these two points was considered as linear and the upper segment as curvilinear. No mathematical description of the lowest segment was used and, therefore, the model only described the P_{dyn}/V curve above the LIP. The mathematical model is described in the Appendix.

Static pressure-volume curves

The static curves (P_{st}/V) were recorded according to the flow interruption principle, which is based on interruption of the inspiratory flow at increasingly larger breaths, as described in details elsewhere [21].The insufflated Vt was automatically increased stepwise to cover volumes from zero to about 25 ml/kg of body weight. The computer forced the ventilator to ZEEP during the measurement of the "study breaths". The static pressure was read 3 s into a post-inspiratory pause following the insufflation. This latency is long enough to allow visco-elastic pressure to decay to an insignificant value, but not so long that continuing absorption of oxygen leads to a volume change [22]. P_{st}/V curves were then constructed by plotting the volume versus the elastic recoil pressure of the respiratory system for each interrupted breath. A single P_{st}/V curve was obtained from, on average, 20–25 "study breaths". The mathematical analysis of the P_{st}/V curve was made using the equation previously described.

Protocol

Routine care, such as suctioning, was performed immediately before the study. The absence of leaks in the circuit was ensured by the establishment of an airway pressure drop of less than 0.1 cmH_2O/s towards the end of a 10 s post-inspiratory pause.

Patients were studied after 30 min of mechanical ventilation at two levels of Vt: with a tidal ventilation of 10–12 ml/kg and then with a low Vt of 5–6 ml/kg of actual BW; the low Vt was accompanied by a reduction in minute ventilation. In these two Vt conditions, P/V curves were recorded successively with the static and dynamic methods. For the latter, two flows were used: the first P_{dyn}/V curve was traced with an insufflation of 6 s and was followed, in the first seven patients, by a second P_{dyn}/V curve recorded with an insufflation of 3 s. The static P/V curve was then recorded. Thirty minutes elapsed between the reduction of the Vt and the new set of measurements.

Statistical analysis

The results are expressed as means ± SD. The values of C_{st}/C_{dyn}, LIP_{st}/LIP_{dyn}, UIP_{st}/UIP_{dyn} determined at Vt 10–12 ml/kg and 5–6 ml/kg were compared by a Wilcoxon paired test. A p less than 0.05 was considered significant. The relationship between compliance, LIP and UIP obtained with static and dynamic methods was assessed by linear regression analysis. The distribution of error was assessed according to the method proposed by Bland and Altman [23].

Results

No significant difference in UIP was found between the static and the dynamic methods. At Vt 10–12 ml/kg, the static and dynamic UIPs were 22.4±4.4 cmH_2O and 22.1±4.5 cmH_2O (p=0.86), respectively; at Vt of 5–6 ml/kg the static and dynamic UIPs were 26.6±4.1 cmH_2O and 25.5±5 cmH_2O (p=0.34), respectively. A linear

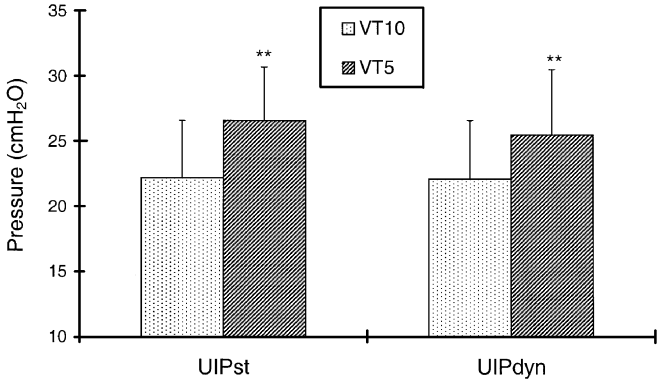

Fig. 2 Upper inflection point identified in both static and dynamic recordings during two ventilatory settings

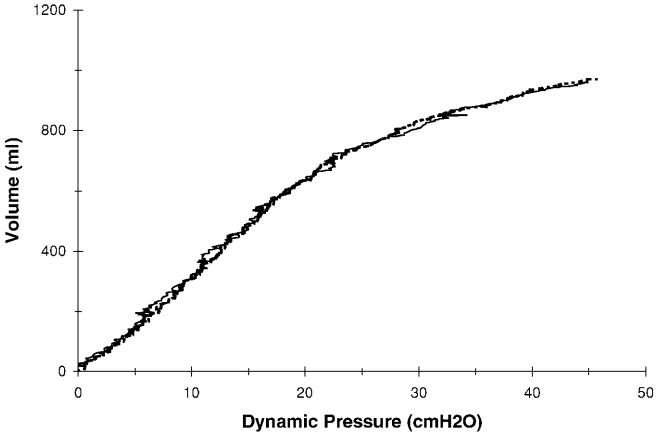

Fig. 3 Two superimposed dynamic pressure-volume curves recorded with an insufflation of either 3 or 6 s

Table 2 Ventilation with a tidal volume of 10–12 ml/kg. Individual values of intrinsic positive and expiratory pressure (*PEEPi*), peak pressure (*Ppeak*), plateau pressure (*Pplat*), mean pressure (*Pmean*), compliance (*Cst* static compliance, *Cdyn* dynamic compliance), lower inflection point (*LIPst* static lower inflection point, *LIPdyn* dynamic lower inflection point) and upper inflection point (*UIPst* static upper inflection point, *UIPdyn* dynamic upper inflection point). (*ND* no LIP or UIP could be identified)

Patients	PEEPi (cmH_2O)	P_{peak} (cmH_2O)	P_{plat} (cmH_2O)	P_{mean} (cmH_2O)	Cst (ml/cmH_2O)	Cdyn (ml/cmH_2O)	LIPst (cmH_2O)	LIPdyn (cmH_2O)	UIPst (cmH_2O)	UIPdyn (cmH_2O)
1	1.2	50	46	10	34	25	ND	ND	25	25
2	2.1	32	27	9	28	30	11	10	33	31
3	0.5	43	31	11	40	38	9	8	23	25
4	1.3	37	30	10	57	60	8	8	25	20
5	3.8	50	39	12	46	50	14	10	25	26
6	3.1	48	37	11	60	60	7	8	ND	ND
7	1.8	53	40	13	33	33	ND	ND	18	16
8	2.7	48	37	12	40	36	6	6	17	17
9	0.5	45	33	10	50	50	4	4	18	18
10	1.8	53	40	16	40	40	ND	ND	13	13
11	2.8	45	34	11	28	32	8	8	15	16
12	4	42	33	10	44	33	11	12	22	26
13	1.4	45	38	13	32	35	10	10	20	20
Mean	2.1	45.4	33.4	9.8	41	40.7	8.8	8	22.2	22.1
± SD	1.1	6	10.4	4.3	10	11.5	2.8	2	4.4	4.5
p value					0.81		0.50		0.86	

regression of value of UIP at Vt 10–12 ml/kg and at Vt 5–6 ml/kg offered the following relationship: UIP_{st}/UIP_{dyn} : R =0.934.

A significant difference in UIP was found, depending on the Vt. In the static condition, UIP at Vt 10–12 ml/kg and at Vt 5–6 ml/kg were 22.2±4.4 cmH_2O and 26.6±4.1 cmH_2O (p<0.005), respectively. In dynamic recordings, UIP at 10–12 ml/kg and at Vt 5–6 ml/kg were 22.1±4.5 cmH_2O and 25.5±5 cmH_2O (p<0.005), respectively (Fig. 2).

In the first seven patients, no difference was observed between the P_{dyn}/V curves obtained with two different insufflation times (3 and 6 s). Accordingly, the subsequent P_{dyn}/V curves were recorded only with an insufflation time of 6 s. In Fig. 3, P_{dyn}/V curves of a representative patient, recorded during insufflations of 6 and 3 s, are superimposed.

In Table 2 and Table 3, the dynamic and static values of compliance, LIPs and UIPs measured at Vt of 10–12 and 5–6 ml/kg are reported. LIP was not identified on static and dynamic recordings in three patients for either level of ventilation. At Vt 10–12 ml/kg the UIP was identified with the two methods in all patients but one. At Vt 5–6 ml/kg, UIP was not identified in three patients.

The levels of LIP and UIP and compliance values were similar when comparing static and dynamic methods. The linear regression performed with values of compliance, LIP and UIP, gave the following regression lines: C_{st}/C_{dyn}: R =0.901; LIP_{st}/LIP_{dyn}: R =0.903;

Table 3 Ventilation with a tidal volume of 5–6 ml/kg. Individual values of intrinsic positive end-expiratory pressure (*PEEPi*), peak pressure (*Ppeak*), plateau pressure (*Pplat*), mean pressure (*Pmean*), compliance (*Cst* static compliance, *Cdyn* dynamic compliance), lower inflection point (*LIPst* static lower inflection point, *LIPdyn* dynamic lower inflection point) and upper inflection point (*UIPst* static upper inflection point, *UIPdyn* dynamic upper inflection point) (*ND* no LIP or UIP could be identified)

Patients	PEEPi (cmH_2O)	P_{peak} (cmH_2O)	P_{plat} (cmH_2O)	P_{mean} (cmH_2O)	Cst (ml/cmH_2O)	Cdyn (ml/cmH_2O)	LIPst (cmH_2O)	LIPdyn (cmH_2O)	UIPst (cmH_2O)	UIPdyn (cmH_2O)
1	1.2	23	22	6	25	28	ND	ND	30	30
2	1.8	19	17	5	28	25	11	10	ND	ND
3	0.5	25	19	6	40	30	8	8	31	25
4	1.1	20	16	5	60	50	8	8	ND	ND
5	3	30	20	7	47	50	11	10	30	32
6	3.1	20	19	5	66	60	7	8	ND	ND
7	1.6	28	25	7	33	33	ND	ND	20	20
8	2.7	30	20	8	36	40	6	6	26	20
9	0.5	25	20	5	50	50	6	6	21	19
10	1.1	33	22	8	40	40	ND	ND	15	15
11	2.1	33	20	6	30	30	7	9	18	20
12	3.5	20	18	5	38	30	8	12	32	32
13	1.1	25	20	8	30	35	6	10	25	25
Mean	1.8	25.4	19.8	6.2	40.2	39.2	7.8	8.3	26.6	25.5
± SD	1	5	2.3	1.2	12.4	11	1.4	1.5	4.1	5
p value					0.26		0.17		0.34	

UIP_{st}/UIP_{dyn}: R =0.934. The bias for compliance (C_{st}/C_{dyn}) was 1.23 ml/cmH_2O with limits of agreement of ±4.92 ml/cmH_2O (+6.14 and –3.69); the bias for LIP (LIP_{st}/LIP_{dyn}) was 0.04 cmH_2O with limits of agreement of ±1.78 cmH_2O (+1.81 and –1.73). The bias for UIP (UIP_{st}/UIP_{dyn}) was –0.23 cmH_2O with limits of agreement of ±3.54 cmH_2O (+3.32 and –3.78).

Discussion

The main results of this study are as follows. In ARDS patients, the existence and the level of UIP were independent of the technique used since interruption and continuous flow techniques with different insufflation times gave similar results. The pressure level of the UIP, however, was modified by previous different modes of ventilation: this pressure level was lower when the previous Vt was high, and higher with a small Vt.

The dynamic inflation technique is an attractive alternative to the time-consuming recording and analysis procedure of the multiple occlusions technique. The dynamic method, being fast and easy to use and requiring no extra equipment for tracing the curve, is particularly suitable for intensive care settings. One recording takes about 30 s and can be fully automated. Subsequent analysis takes only 2 min with the procedure used in this study. Its feasibility and accuracy have already been studied [9, 24].

The respiratory system P/V curve assesses mechanical characteristics of lungs and chest wall together. Roupie et al. [6] partitioned the chest wall and the lung components by measuring esophageal pressure in seven ARDS patients. In all of them, UIP was found to depend solely on lung characteristics, with no involvement of the chest wall. As shown by recent studies [15, 25, 26], the influence of the chest wall seems minimal in medical ARDS patients in whom the abdominal pressure is not increased, while it has a great potential influence in surgical ARDS patients, especially after trauma or abdominal surgery. Since we have used the P/V curve recordings as a bedside tool to estimate mechanics and adjust mechanical ventilation, we did not measure esophageal pressure, which is difficult to perform in daily clinical monitoring. However, to minimize any possible role of the chest wall in this study, we included only medical patients, who were continuously paralyzed. Patients with known or suspected chest wall abnormalities were excluded from our analysis. However, since our patients were medical ARDS, our results have to be extrapolated with caution to other populations.

By and large, the way the UIP was determined in this study did not influence its value. A good agreement between UIP values obtained with the interruption and the continuous flow techniques with a 5–6 ml/kg Vt was observed. UIP was not evidenced on P/V curves yielded by both methods in patients 2, 4, 6 (Table 3). Patient 2 was the only one that did not show an UIP with a 10–12 ml/kg Vt (Table 2). Increasing the speed of insufflation during the continuous flow method (by reducing the insufflation time from 6 to 3 s) did not modify the level of UIP. Indeed, P/V curves were so similar (Fig. 3) that we stopped recording the 3s insufflations after the 7^{th} patient.

The only difference we noticed between the interruption and the continuous flow methods was that the P/V curve above the UIP was more flat or horizontal, suggesting the role of visco-elastic pressure in dynamic con-

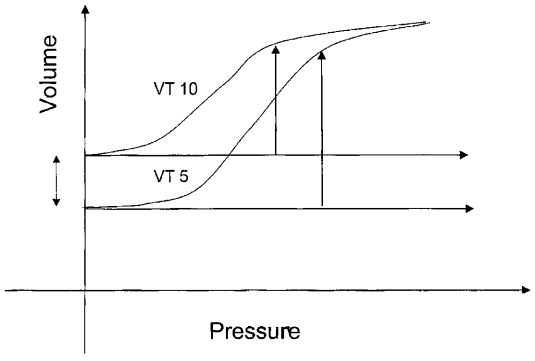

Fig. 4 Differences in upper inflection point in curves at the two different tidal volumes

ditions at high volume [9, 24]. Such data confirm our previous comparison of the two methods [9], but emphasize that the UIP is independent of the method used. In a previous study [9], UIP was more often present with the dynamic method in non-ARDS patients. Recently Jonson et al. [24] reported a lower value of compliance and LIP measured at ZEEP with the dynamic method compared to the static method. In both studies these differences found between the static and dynamic methods had little clinical significance, however.

The levels of UIPs obtained in this study – 27 cmH_2O with 5–6 ml/kg and 22 with 10–12 ml/kg, using the static method – are in accordance with earlier publications. In a previous study [10], UIP was identified in nine out of ten ARDS patients, at a mean value of about 25 cmH_2O under static and dynamic conditions. Roupie et al. [6] have documented UIP in a group of ARDS patients at a mean value of about 26 cmH_2O (range 18–40 cmH_2O) and Brunet et al. [27] found UIP in a narrower range of values, between 28 and 32 cmH_2O.

As shown in Fig. 2, the mean value of UIP was significantly lower with 10–12 ml Vt than with 6 ml Vt using both methods. An initial hypothesis may be that mechanical ventilation with higher Vt recruits more of the lung predisposed to end-expiratory collapse, displacing upwards the total P/V curve, which starts from a higher elastic recoil position (Fig. 4). This is in accordance with several recent reports [7, 24, 28, 29, 30]. Moreover, several authors [31, 32] have shown that ventilatory setting and, in particular, recruitment maneuver can markedly influence the end-expiratory volume. This is one of the reasons why we do not perform a recruitment maneuver before our recordings.

The influence of Vt has already been described by Cheney [33]; he measured an augmented FRC while increasing Vt in dogs injected with oleic acid. PEEP plays the same role, by increasing end-expiratory lung volume and displacing the P/V curve upwards. It may be the reason why Mergoni et al. [15] reported such low values of UIP, since their P/V curves were traced starting from a PEEP of 15 cmH_2O. This would explain a change in the volume of the UIP, however, but may not explain a decrease in pressure with high Vt. Our hypothesis is supported by Richard et al. [34] who recently observed, in 15 ARDS patients, that a small Vt of 6 ml/kg, compared to a Vt of 10 ml/kg, induced a de-recruitment that was reversed by increasing PEEP. The other explanation may be that with more lung being recruited, the end of recruitment may be reached sooner. This hypothesis would fit better with the notion that UIP is essentially a marker of the end of recruitment. Moreover, the size of the Vt may impact on surfactant function and may play a role in these findings. Lastly, it has to be mentioned that UIP can be affected by thoracic blood volume and fluid status due to the higher pressure reached. This is a possibility that needs further study.

This study also confirms the results of Roupie [6] about the relationship between end-inspiratory plateau pressure and UIP in ARDS, since with a 10–12 ml/kg Vt the end-inspiratory plateau pressure was above the UIP in all patients but two while the end-inspiratory plateau pressure was below UIP in all patients but one with a 5–6 ml/kg Vt.

It was beyond the scope of this study to assess the clinical relevance of determining UIP, since we compared several ways of tracing P/V curves without collecting data on oxygenation or outcome. Such studies would necessitate prolonged periods of observation and the inclusion of many more patients. However, it is worth trying to put UIP determination in the perspective of mechanical ventilation for ARDS. On the one hand, recent studies have reported successful utilization of Vt limitation using an upper limit identified by UIP [8]. On the other, convincing models [16, 17] seem to indicate that UIP corresponds to the end of recruitment and not necessarily to over-distension. However, these two concepts may not be as opposed as they seem to be. Recruitment is certainly not an all or nothing phenomenon, as once believed, since many recent studies have reported that recruitment goes on continuously during tidal excursion [24, 35]. The same applies to over-distension, which starts relatively low in the vital capacity and increases when airway pressure is augmented, either by PEEP or tidal excursion. In 25 ARDS patients, Dambrosio et al. [36] showed that, when Vt was increased from 6 to 10, end-expiratory pressure surpassed UIP, which corresponded to obvious over-distension on CT scanning, while recruitment did not continue to progress. Accordingly, determination of UIP could indicate the upper limit for end-inspiratory plateau pressure, and help to adjust PEEP and Vt in severe ARDS. This needs to be further confirmed in appropriately designed clinical trials.

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Appendix

$$\text{LIPtoUIP}: P_{dyn}(V) = P_{dyn0} + \frac{V}{C_{lin}}$$

$$\text{AboveUIP}: P_{dyn}(V) = P_{dynUIP} + \frac{V_{max} - V_{UIP}}{C_{lin}} \cdot \cdot \ln\left(\frac{V_{max} - V_{UIP}}{V_{max} - V}\right)$$

The relationship of the linear segment between LIP and UIP is described by the coefficients $P_{dyn\ 0}$ and C_{lin}. $P_{dyn\ 0}$ is the intercept of the extrapolated linear segment with the pressure axis and C_{lin} is compliance over the linear segment. Accordingly, the UIP was defined as the point where the statistical analysis indicated the start of the deviation of the P_{dyn}/V curve from a straight line. Additional volume increments lead to pressure increments from $P_{dyn\ UIP}$, according to the second term in the lower part of the equation. This implies that compliance falls linearly with additional volume from its value of linear compliance (C_{lin}) until it reaches zero at maximum distension of the lungs at maximum volume (V_{max}). The equation for the segment above UIP satisfies the equation of Salazar and Knowles [37] and has been applied in recent studies [24, 38, 39]. The pressure at the lower inflection point (P_{LIP}), was defined from the point of the P_{dyn}/V curve at which the measured pressure deviated from the mathematical model by more than 0.5 cmH_2O.

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