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Low flow inflation pressure-time curve in patients with acute respiratory distress syndrome

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Abstract *Objective*: In mechanically ventilated patients with ARDS, determination of the lower (LIP) and upper (UIP) inflection points of the static pressure-volume curve (P-V) is crucial for planning ventilatory strategies. Recently, a simple new method was proposed for measuring the P-V curve by inflating the lung with constant low flow [14]. We hypothesized that during low flow inflation LIP and UIP might be determined using the pressure-time curve (P-T) instead of P-V. *Methods*: Eleven paralyzed patients with ARDS were studied. During volume control ventilation the patients were allowed to reach passive functional residual capacity (FRC) and then ventilator frequency, inspiratory to total breath duration ratio and tidal volume (V_T) were set to 5 breaths/min, 80% and 500 or 1500 ml, respectively. With these settings, constant inspiratory flow (V'_I) was administered for 9.6 s and ranged, depending on V_T, between 0.05 and 0.15 l/s. P-V and P-T were obtained at two levels of positive end-expiratory pressure (PEEP; 0 and 10 cmH_2O), with V'_I being achieved either fast (< 0.1 s, minimum delay) or slowly (0.4 s, maximum delay). *Results*: With minimum flow delay for a given experimental condition, the shape of the P-T did not differ from that of P-V. In all cases P-T correctly identified the presence of LIP and UIP, which did not differ significantly between P-T and P-V. With maximum flow delay, compared to P-V, the initial part of P-T was significantly shifted to the left. P-T did not identify the presence of UIP and LIP in one and two cases, respectively. *Conclusions*: Provided that constant flow is given relatively fast, P-T accurately determines the shape of P-V, as well as the LIP and UIP. Flow delay causes a leftward shift of the initial part of P-T, masking the presence of LIP and UIP in some cases.

Key words Pressure-volume curve · Lower inflection point · Upper inflection point · Compliance · Recruitment · Over-distension

Introduction

In patients with acute respiratory distress syndrome (ARDS) the static pressure-volume (P-V) curve of the respiratory system is a valuable tool that may help the physician to set the ventilator properly. Usually, in patients with ARDS, the inflation limb of the P-V curve of the respiratory system has a sigmoidal shape, with a lower (LIP) and upper (UIP) inflection point [1, 2]. It has been proposed that these two points identify a safe range of pressures during mechanical ventilation. Animal, as well as human, data indicate that ventilating these patients with pressures kept within this range may reduce the so called "ventilator-induced lung injury" [3, 4, 5, 6, 7, 8, 9], an important factor of increased morbidity and mortality in patients with ARDS [10]. In-

deed, it has been shown that the mortality of ARDS was significantly reduced if the patients were ventilated based on information obtained with the P-V curve [11]. Recently, Ranieri et al. [9] have shown that ventilating ARDS patients with positive end-expiratory pressure (PEEP) above LIP and end-inspiratory static pressure below UIP significantly reduced the pulmonary and systemic inflammatory responses, as suggested by the decrease in cytokine levels in bronchoalveolar lavage and plasma. It follows that determination of LIP and UIP should be an integral part of the lung protective strategy in mechanically ventilated patients with ARDS.

Until recently P-V curves were recorded using time-consuming and cumbersome bedside techniques [1, 2, 12, 13]. Lu et al. [14] introduced a simple automated method for measuring P-V curves in critically ill patients. These authors performed P-V curves by setting the ventilator on volume control mode, the inspiratory to total breath duration ratio (T_I/T_{TOT}) at 80 %, respiratory frequency at 5 breaths/min and the tidal volume (V_T) at 500 or 1500 ml, given with a square-wave flow-time profile. With these peculiar ventilator settings the constant inspiratory flow (V'_I) ranged, depending on V_T, between 3 and 9 l/min and was administered for 9.6 s. The resulting P-V curve did not differ from that obtained using the reference methods of the super-syringe and inspiratory occlusions. The slopes of P-V curves and the LIP were similar for all methods, indicating that the resistive pressure generated by administering a constant flow equal to or less than 9 l/min is of no clinical significance, at least in patients without obstructive lung disease. Similar results have also been reported by Rodriquez et al. [15] who obtained the P-V curve by inflating the lung with a constant flow of 7 l/min.

We hypothesized that the shape of the P-V curve obtained with the technique of constant low flow inflation might be determined using the pressure-time (P-T), instead of P-V, relationships. Indeed, provided that flow is given with a square-wave flow-time profile, pressure has a similar relationship with either time or volume. Determination of the shape of the P-V curve from P-T relationship might overcome the problems that several intensive care units have, due to limited financial resources, to record volume during inspiration. Several ventilators do not have on-line waveform tracing capability, making the P-V curve recording quite complicated. On the other hand, recording the P-T curve does not need a ventilator screen and can be performed at the bedside using only a pressure transducer and the screen of the patient's monitor. The aim of the present study, therefore, was to validate the P-T technique for determining the clinically relevant pressure points of the P-V curve. The LIP and UIP obtained from the P-T curve were compared to those obtained from the P-V curve. Furthermore, because some ventilators are not able to provide constant flow immediately, we recorded the P-T curve after introducing a time delay in achieving this and we examined the effect of this delay on the shape of the curve.

Methods

Eleven consecutive adult patients needing mechanical ventilation, due to ARDS, were studied prospectively. The diagnosis of ARDS was based on American-European Consensus Conference criteria [16]. The protocol was considered as a part of clinical practice and, thus, no informed consent was obtained. Exclusion criteria were a previous history of obstructive lung disease or asthma and the presence of a chest tube with a persistent air leak.

All patients were orotracheally intubated with endotracheal tube no. 8 and ventilated (Siemens, Servo Ventilator 300, Solna, Sweden) on volume control mode using a V'_I and with settings determined by the primary physician. This type of ventilator has the ability to achieve the constant flow in a pre-determined time. The patients were sedated with a continuous infusion of propofol-fentanyl and paralyzed with cis-atracurium. Flow at the airway opening was measured with a heated pneumotachograph (Hans-Rudolf 3700, Kansas, U.S.A.) and a differential pressure transducer (Micro-Switch 140PC, Honeywell, Ontario, Canada) placed between the endotracheal tube and the Y-piece of the ventilator. Flow was electronically integrated to provide volume. Airway pressure (Paw; Micro-Switch 140PC, Honeywell, Ontario, Canada) was measured from a side port between the pneumotachograph and the endotracheal tube. All signals were sampled at 150 Hz (Windaq Instruments, Ohio, U.S.A.) and stored on a computer disk for later analysis.

Protocol

Initially the FIO_2 increased to 100 % and remained at this level throughout the study. The P-T and P-V relationships were examined at two levels of PEEP (0 and 10 cmH_2O), applied sequentially. At each level of PEEP the patients were ventilated for 10–15 min with the initial ventilator settings. At the end of each period, in order to standardize the volume history before recording the P-T and P-V curves, V_T was set at 0.5 l, ventilator frequency at 10 breaths/min and T_I/T_{TOT} at 0.3. Inspiratory flow was given with a square-wave profile. With these settings, the patients were ventilated for five breaths. By decreasing the ventilator frequency to 5 breaths/min the expiration of the 5th breath was prolonged, permitting the patient to reach passive functional residual capacity (FRC), determined by the PEEP level. The following breath was given with a V_T of 500 or 1500 ml, T_I/T_{TOT} of 80 % and ventilator frequency of 5 breaths/min. With these settings the V'_I (50 ml/s when V_T was set at 500 ml, and 150 ml/s when V_T was set at 1500 ml) was administered for 9.6 s. The V'_I was achieved either with the minimum delay (< 0.1 s) or gradually with a delay of 0.4 s (5 % of inspiratory time, maximum delay) (Fig. 1). At each PEEP level and mode of constant flow administration (minimum and maximum delay) three trials with V_T of 500 ml and three with V_T of 1500 ml were performed. Between trials 2–3 min of baseline ventilation were allowed. If, with high volume inflation and no PEEP, end-inspiratory Paw approached or exceeded 50 cmH_2O (± 5 cmH_2O) or a clear-cut reduction of the slope of P-V curve at the end of inspiration was observed, high volume inflation with 10 cmH_2O PEEP was not performed for safety reasons.

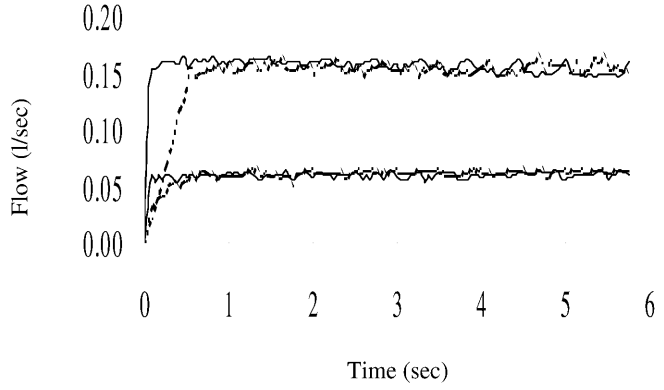

Fig. 1 Flow-time profile in achieving constant inspiratory flow of 0.05 and 0.15 l/s. *Solid lines*: with a minimum flow delay (< 0.1 s), *dashed lines*: with flow delay of 5 % of inspiratory time (maximum flow delay)

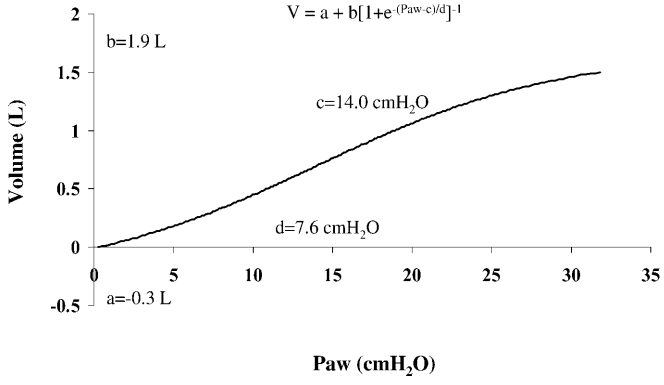

Fig. 2 Pressure-volume curve in a representative patient, described by the sigmoidal equation of Venegas et al. [17] (*V* volume, *Paw* airway pressure, *a, b* lower and upper asymptotes to volume axis, respectively, *c* pressure at the point at which the curvature changes sign, *d* width parameter proportional to the pressure range within which most of the volume change occurs

Data analysis

We thought that modelling of the P-V and P-T curves was necessary in order to define the shape of the curve mathematically and to make possible unbiased statistical comparisons. We decided to analyze each curve using the sigmoidal equation proposed by Venegas et al. [17] of the form:

$$V = a + b\,[1 + e^{-(P-c)/d}]^{-1} \quad (1)$$

where P is the pressure at a given volume (V) above end-expiratory lung volume, a and b correspond to the volume of the lower and upper asymptotes, respectively, c to the pressure at the point at which the curvature changes sign and d to a width parameter proportional to the pressure range within which most of the volume change occurs (Fig. 2). The parameter c is the pressure also at the point of the highest compliance Cmax = (b–a)/4d). It has been shown that Eq. 1 described with excellent accuracy the inflation and deflation limb of the P-V curve in patients with ARDS [17, 18].

Similarly, the shape of the P-T curve was analyzed using the same equation by substituting the volume with time as follows:

$$T = a + b\,[1 + e^{-(P-c)/d}]^{-1} \quad (2)$$

where T is time at pressure P (zero time was defined as the point at which Paw started to increase from the value reached at the end of the prolonged expiration) and a and b correspond to the time of the lower and upper asymptotes, respectively, c to the pressure at which the curvature changes sign and d to a width parameter proportional to the pressure range within which most of the time change takes place.

To facilitate comparison between the P-V and P-T curves, volume and time were expressed as percentages of inflation volume and time, respectively. Therefore, it was possible to interchange the P-V and P-T obtained with this technique. These curves were also analyzed using the sigmoidal equation of Venegas et al. [17] modified as follows:

$$\%\ \text{of inflation volume or time} = a + b\,[1 + e^{-(P-c)/d}]^{-1} \quad (3)$$

where a and b are the lower and upper asymptotes to y axis, respectively, expressed as percentages of inflation volume (for P-V curve) or time (for P-T curve).

In both curves (P-V and P-T) the LIP and UIP were determined as the pressure of maximal upward and downward curvature, respectively. These points can be directly [17, 18] obtained as a function of c and d as follows:

$$LIP = c - 1.317d \quad (4)$$
$$UIP = c + 1.317d \quad (5)$$

Data are presented as means ± SD. The P-V and P-T curves were fitted by Eq. 1, 2 and 3 in a personal computer using the Levenberg-Marquardt iterative algorithm to minimize the sum of squared residuals (Origin software). The algorithm was set to run until the resulting sum of squared residuals changed by less than 0.0001. At this point estimates of parameters a, b, c and d, as well as the best fit coefficient of r^2, were obtained. We considered that LIP was present either in the P-V or P-T curves if the obtained value was above the PEEP level. UIP was considered to be present if the obtained value was less than or within ± 1 cmH_2O of the end inspiratory Paw observed in the corresponding P-V or P-T curves. The values of various parameters obtained by analysis of P-T and P-V curves were compared by mutlifactorial analysis of variance with repeated measurements followed by Tukey's test if the *F* value was significant. A *p* less than 0.05 was considered statistically significant. In patients in whom LIP was identified in the P-V curve, the agreement (bias) between the two methods of calculating the LIP was expressed as the mean of the corresponding differences obtained by the P-V and P-T curves. The limits of agreement were expressed as the mean ± 1.96 SD, and 95 % of the confidence intervals of the bias were calculated according to Bland and Altman [19]. Similar analysis was carried out with UIP.

Results

Six males and five females with a mean age of 61.1 ± 15.4 years were studied. Mean PaO_2/FIO_2 was 119 ± 0.67, whereas the lung injury score [20] averaged

Table 1 Parameters a, b, c and d obtained by the pressure-volume and pressure-time analyses when flow was administered with a minimum delay (*P-V* pressure-volume, *P-T* pressure-time, *a* lower asympote to y axis, *b* upper asymptote to y axis, (% of inflation volume and time, respectively, for P-V and P-T), *c* pressure at the point at which curvature changes sign (cmH_2O), *d* width parameter proportional to the pressure range within most of the volume (for P-V) and time (for P-T) change takes place (cmH_2O)

	PEEP 0				PEEP 10			
	Low volume		High volume		Low volume		High volume	
	P-V	P-T	P-V	P-T	P-V	P-T	P-V	P-T
a	–28.51 ± 18.6	–28.56 ± 18.9	–81.32 ± 177.3	–74.95 ± 176.2	–53.04 ± 22.0	–52.95 ± 25.0	–102.61 ± 58.6	–109.79 ± 65.3
b	189.7 ± 85.4	197.7 ± 101.3	222.9 ± 233.4	229.4 ± 240.9	195.81 ± 57.52	201.70 ± 66.9	216.2 ± 77.8	235.8 ± 94.9
c	12.00 ± 4.3	12.41 ± 5.1	12.60 ± 26.0	13.81 ± 24.0	17.03 ± 1.8	17.35 ± 2.04	15.39 ± 7.6	14.98 ± 8.6
d	5.78 ± 2.5	5.90 ± 2.4	18.01 ± 24.8	19.06 ± 27.3	6.53 ± 3.0	6.72 ± 3.3	14.96 ± 5.4	16.06 ± 6.0

Values are mean ± SD

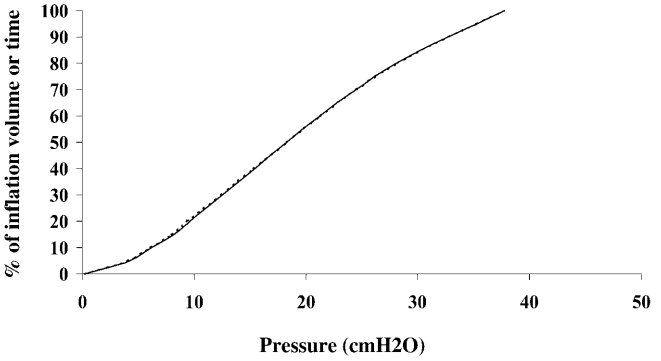

Fig. 3 Average pressure-volume *(solid lines)* and pressure-time *(dashed lines)* curves when inspiratory flow of 0.15 l/s (1500 ml inspiratory volume) was administered with a minimum flow delay (< 0.1 s) at zero PEEP. Volume and time were expressed as percentages of total inflation volume and inspiratory time, respectively

2.49 ± 0.67 points. Pneumonia was the cause of ARDS in five patients, aspiration in three and septic shock in three. Static end-inspiratory compliance of the respiratory system (Cst,rs) was 48.3 ± 4.8 ml/cmH_2O, whereas total resistance of the respiratory system (Rrs) amounted to 6.6 ± 0.8 cmH_2O·l·s. Cst,rs and Rrs were determined using the occlusion technique [21]. For safety reasons, high volume inflation with PEEP was not performed in 5 out of 11 patients. Therefore, the results with this condition pertain to six patients.

In all cases and independent of conditions studied, the r^2 value was above 0.98, indicating that the P-V and P-T curves were adequately described by the Eq. 1, 2 and 3. As expected, for a given condition the parameters c and d obtained from equations 1 and 2 (i.e. when volume and time were absolute values) were similar to those obtained from equation 3 (i.e. when volume and time were expressed as % of V_T and inflation time, respectively).

Pressure-volume and pressure-time curve analysis

With minimum flow delay

In all cases the constant flow was achieved in less than 0.1 s, corresponding to zero PEEP, to a pressure of 0.8 ± 0.3 and 2.3 ± 0.5 cmH_2O, respectively, with low and high volume. Independent of volume of inflation and PEEP levels, the parameters a, b, c and d, as well as the LIP and UIP obtained by the Eq. 3, did not differ between P-T and P-V curve analysis. As a result, the shape of the P-V curve was similar to that of the P-T one (Table 1, Fig. 3).

At zero PEEP and with low volume nine patients exhibited LIP. This was evident on both curves. In these patients LIP obtained by analyzing the P-V (LIP_{P-V}) and P-T (LIP_{P-T}) curve averaged 5.39 ± 2.2 and 5.77 ± 2.7 cmH_2O, respectively. In one patient LIP was identified neither in the P-V curve nor in the P-T curve, while in another LIP by both methods was close to zero. In these two patients LIP was not identified with high volume inflation. In the remaining nine patients, with high volume, LIP was present either on P-V or P-T, averaging 7.75 ± 3.8 cmH_2O and 7.68 ± 4.1 cmH_2O, respectively, for LIP_{P-V} and LIP_{P-T}. With PEEP and low volume four patients exhibited LIP, identified on both curves. In these patients LIP was slightly above the PEEP level. In the remaining patients neither the P-V nor the P-T analysis identified LIP. With high volume inflation and PEEP, only one patient exhibited LIP. This was slightly above PEEP and observed on both curves.

At zero PEEP and with low inflation volume, UIP_{P-V} and UIP_{P-V} were at least 1 cmH_2O higher than the pressure achieved at the end of inflation in all but three patients. At zero PEEP and high inflation volume, UIP was identified in seven patients. This was evident on both curves. With PEEP and low volume inflation five patients exhibited UIP either by P-V or P-T curve analysis. UIP was identified on both curves in five out of six patients in whom high volume inflation, at 10 cmH_2O of PEEP was performed.

Table 2 Minimum flow delay. Mean difference of lower and upper inflection points obtained by pressure-volume (P-V) and pressure-time (P-T) curve analyses, limits of agreement of the difference (1.96 ± SD of the mean difference) and 95 % confidence interval for the bias (LIP_{P-V} lower inflection point obtained by P-V curve analysis, LIP_{P-T} lower inflection point obtained by P-T curve analysis, UIP_{P-V} upper inflection point obtained by P-V curve analysis, UIP_{P-T} upper inflection point obtained by P-T curve analysis)

	Low volume inflation		
	Mean difference	Limits of agreement	95 % Confidence interval for bias
LIP_{P-V}-LIP_{P-T} (cmH_2O)	–0.10	0.96 to –1.16	0.19 to –0.39
UIP_{P-V}-UIP_{P-T} (cmH_2O)	–0.29	0.28 to –0.85	–0.05 to –0.52
	High volume inflation		
	Mean difference	Limits of agreement	95 % confidence interval for bias
LIP_{P-V}-LIP_{P-T} (cmH_2O)	0.06	1.03 to –0.90	0.40 to –0.28
UIP_{P-V}-UIP_{P-T} (cmH_2O)	–0.81	0.64 to –2.25	–0.34 to –1.28

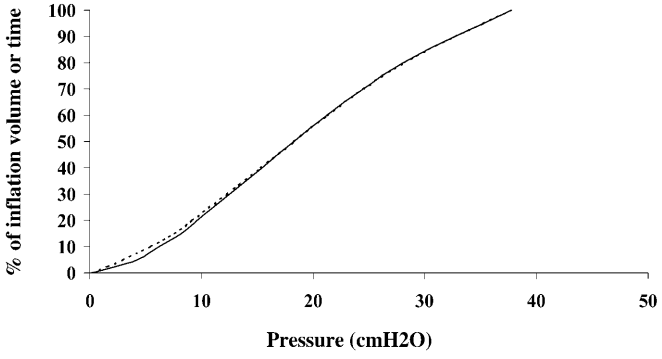

Fig. 4 Average pressure-volume *(solid lines)* and pressure-time *(dashed lines)* curves when inspiratory flow of 0.15 l/s (1500 ml inspiratory volume) was administered with a maximum flow delay at zero PEEP. Volume and time were expressed as percentages of total inflation volume and inspiratory time, respectively

In patients in whom LIP or UIP was identified on the P-V curve, the mean difference between LIP (LIP_{P-V}-LIP_{P-T}) and UIP (UIP_{P-V}-UIP_{P-T}) obtained by P-V and P-T curve analyses, the limits of agreement and the 95 % confidence interval for the bias (mean) are shown in Table 2.

With maximum flow delay

The constant flow was achieved in 0.40 ± 0.05 and 0.49 ± 0.06 s, respectively, with low and high volume inflation ($p < 0.05$). With zero PEEP the corresponding pressure was 1.1 ± 0.5 and 2.9 ± 0.8 cmH_2O, respectively, with low and high volume. With low volume inflation, for a given percentage of inflation volume and time, Paw in the P-T curve was slightly lower than that in the P-V at the beginning of inflation. The maximum difference was at approximately 5 % of inflation volume and time (25 ml and 0.48 s, respectively); at 5 % of inflation volume and time, mean Paw was 1.9 ± 0.7 and 1.6 ± 0.6 cmH_2O, respectively ($p < 0.05$). With high volume inflation and no PEEP the difference in Paw between the P-V and P-T curves at the initial part of the curve was considerably higher than the corresponding value with low inflation volume (Fig. 4). At 5 % of inflation volume and time (75 ml and 0.48 s, respectively) mean Paw was 4.2 ± 1.84 and 3.0 ± 1.1 cmH_2O, respectively.

Application of PEEP did not change the initial difference in Paw between the P-V and P-T curves observed with the maximum flow delay. With low volume inflation at 5 % of inflation volume and time, Paw was 11.4 ± 0.5 and 11.1 ± 0.6 cmH_2O, respectively, while the corresponding values with high volume inflation were 12.9 ± 0.7 and 11.7 ± 0.8 cmH_2O ($p < 0.05$). With low volume inflation, despite the significant initial leftward shift of P-T curve, the shape of the P-T curve did not differ from that of P-V. Only in one case did the P-T curve analysis not identify the presence of LIP, which, however, was close to zero. With high volume inflation the shape of the curve differed significantly between P-T and P-V (Table 3). In one case P-T did not identify the LIP and in another the UIP.

In patients in whom LIP or UIP was identified on the P-V curve, the mean difference between LIP (LIP_{P-V}–LIP_{P-T}) and UIP (UIP_{P-V}–UIP_{P-T}) obtained by P-V and P-T curve analyses, the limits of agreement and the 95 % confidence interval for the bias (mean) are shown in Table 4. With high volume inflation the range of the limits of agreement and 95 % confidence interval was wider than these with low volume.

Discussion

The main finding of the study was that the P-T curve obtained with low constant flow inflation technique, provided that the constant flow was achieved relatively fast, may reliably describe the shape of the P-V curve, as well as the effect of PEEP on the curve shape. On

Table 3 Parameters a, b, c and d obtained by the pressure-volume (P-V) and pressure-time (P-T) analyses when flow was administered with a maximum delay (see Table 1 for abbreviations)

	PEEP 0				PEEP 10			
	Low volume		High volume		Low volume		High volume	
	P-V	P-T	P-V	P-T	P-V	P-T	P-V	P-T
a	–27.10 ± 17.1	–28.39 ± 18.1	–64.47 ± 133.1	–73.70 ± 148.8	–52.09 ± 20.1	–53.90 ± 25.8	–75.34 ± 39.7	–107.27 ± 61.2*
b	191.3 ± 83.5	204.8 ± 105.5	204.5 ± 186.6	234.7 ± 215.7*	196.4 ± 56.2	205.9 ± 70.8	203.8 ± 43.5	252.6 ± 82.4*
c	11.97 ± 4.3	12.53 ± 5.3	14.57 ± 17.1	15.31 ± 20.2	16.99 ± 1.7	17.32 ± 2.04	18.49 ± 5.2	16.23 ± 7.4
d	5.67 ± 2.5	5.96 ± 2.5	16.22 ± 21.4	18.77 ± 24.6	6.43 ± 3.0	6.83 ± 3.5	12.89 ± 4.2	16.46 ± 7.1*

Values are mean ± SD
* Significantly different from the corresponding values of P-V curve

Table 4 Maximum flow delay. Mean difference of lower and upper inflection points obtained by pressure-volume and pressure-time curve analyses, limits of agreement of the difference (1.96 ± SD of the mean) and 95 % confidence interval for the bias (see Table 2 for definitions of abbreviations)

	Low volume inflation		
	Mean difference	Limits of agreement	95 % Confidence interval for bias
$LIP_{P\text{-}V}$-$LIP_{P\text{-}T}$ (cmH_2O)	–0.05	1.34 to –1.45	0.32 to –0.43
$UIP_{P\text{-}V}$-$UIP_{P\text{-}T}$ (cmH_2O)	–0.44	0.56 to –1.43	–0.02 to –0.85
	High volume inflation		
	Mean difference	Limits of agreement	95 % Confidence interval for bias
$LIP_{P\text{-}V}$-$LIP_{P\text{-}T}$ (cmH_2O)	0.58	4.33 to –3.16	1.91 to –0.75
$UIP_{P\text{-}V}$-$UIP_{P\text{-}T}$ (cmH_2O)	–1.18	2.09 to –4.45	–0.12 to –2.24

the other hand, introducing a flow delay caused a leftward shift of the P-T curve, masking the presence of LIP and UIP in some cases.

In order to avoid bias, we decided to analyze the P-V and P-T curves using the sigmoidal equation proposed by Venegas et al. [17]. Although this equation has several limitations, particularly in terms of not containing enough data along one of the asymptotes of the sigmoid, it describes with excellent accuracy the P-V relationship in patients with ARDS [17, 18]. Furthermore, the lack of data along one of the asymptotes of the sigmoid should mainly affect the parameters a or b, which are not used in the calculation of LIP and UIP. With the appropriate acquisition system and software programme the data can be processed and analyzed using this equation in less than 2 min. However, our study does not intend to propose this equation for clinical practice; it was simply used for unbiased statistical comparison. Alternatively, determination of the relevant points may be performed by visual inspection of the P-T curve, which can be frozen on a patient's bedside monitor. Notwithstanding that clinicians have difficulty reproducing the points of interest [18] the fact that the curve in our study was obtained by continuously recording pressure and not by fitting a number of points might permit better curve resolution, assisting the visual inspection of the curve to some extent. Indeed, Harris et al. [18] have shown that the ability of clinicians to determine the LIP increased with increasing data points. Nevertheless, further studies are needed to resolve this issue.

The LIP and UIP were determined using the technique of low flow (< 0.15 l/s) inflation and not the conventional methods of super-syringe or end-inspiratory occlusion [1, 13]. Two recent studies have shown, in patients with relatively low airway resistance, that the P-V curve obtained with low flow inflation (< 0.15 l/s) did not differ from that determined by conventional methods [14, 15]. Therefore, provided that patients with normal or slightly elevated airway resistance are studied, P-V curves obtained with the low inflation technique are reliable and may be used instead of the time-consuming conventional techniques. In the present study patients with airway obstruction were excluded and thus LIP identified with quasi-static P-V curves should be very similar to that identified with the other methods. This hypothesis is further supported by the finding that PEEP eliminated or greatly minimized the LIP, indicating that the presence of the LIP was not the result of the initial shift of the curve due to resistive pressure.

The LIP and UIP were defined as the pressure at the maximal upward and downward curvature of the curve (P-V and P-T), respectively. It is not known if this definition is clinically optimal. In addition, P-V and P-T curves were referred to the total respiratory system and, thus,

the contribution of lung and chest wall to LIP and UIP is unknown. It has been shown that in patients with ARDS the chest wall may influence the value of LIP to a variable extent [22]. On the other hand, UIP mainly reflects lung properties [22]. Nevertheless, it is unlikely that UIP obtained using low inflation volume and no PEEP was the pressure above which over-distension occurs. Indeed, in all cases UIP was considerable higher when PEEP was added or high volume inflation was performed, indicating that low volume inflation at zero PEEP is not able to describe accurately the point at which the patient is at risk for over-distension. The interpretation of UIP is further complicated by the possibility that the slope of the P-V curve may be decreased because of diminishing the lung recruitment and not of over-distension [23]. Similarly, lung recruitment may occur far above the LIP, also making its interpretation problematic [23, 24]. However, the purpose of the study was to compare the shape of P-V and P-T curves and not to extrapolate the LIP and UIP as defined in clinical practice. The mathematically defined LIP and UIP permitted unbiased comparison of points between P-V and P-T curves, which might be of clinical significance.

The ventilator we used was able to achieve the constant flow in pre-determined time. Thus, it was possible to study the effects of different time delays on the P-T curve. We chose a minimum delay of less than 0.1 s to approach an ideal situation and a maximum of 0.4–0.5 s to simulate the function of several ventilators with which there is a considerable delay in achieving the constant flow.

On both inflation volumes and PEEP levels the P-T curve obtained with a minimum flow delay had a shape comparable to that of the corresponding P-V curve. The parameters describing the whole curve as well as the points of maximal upward and downward curvature, defined as LIP and UIP, respectively, did not differ significantly between the P-T and P-V curve analyses. Furthermore, in all patients and independent of conditions studied (inflation volume and PEEP) the P-T curve correctly identified the presence, or lack of this, of the LIP and UIP, whereas the difference between the two methods was of no clinical significance.

The time delay in achieving the constant flow which was introduced had the consequence that, at the beginning of inflation for a given percentage of inflation volume or time, the Paw in the P-T curve was significantly lower than that in the P-V curve. This resulted in an appreciable shift to the left of the initial part of the curve. Compared to low volume inflation, this difference was considerably higher with high volume due to the approximately 0.1 s greater time delay in achieving constant flow. The greater initial leftward shift with high volume inflation caused the shape of the P-T curve to differ significantly from that of the corresponding P-V one at both PEEP levels, resulting in a relatively wide range of agreement of UIP or LIP obtained by P-T and P-V curve analyses. On the other hand, with low volume inflation, and despite the flow delay, the P-T curve had a comparable shape to the P-V curve. It follows that, with a time delay less than 0.4 s in achieving V'_I, P-T curves might be used instead of P-V curves for determination of LIP and UIP.

We observed that LIP determined from the P-V curve using low volume inflation was considerably lower than that obtained using high volume in five patients without PEEP. This could be due to higher resistive pressure because of higher flow and/or to continuous increase in the slope of P-V (and P-T with a minimum time delay) curve above 500 ml. To differentiate between these two possibilities we analyzed the P-V curve constructed with high volume in these five patients, but using only the first 500 ml. In this analysis LIP was approximately 1 cmH_2O higher than that of the P-V curve of low volume inflation, indicating that the higher difference in LIP was due to continuous increase in the slope above 500 ml. This continuous increase was probably due to ongoing recruitment of alveoli above the LIP [24, 25].

The P-T curve can easily be obtained without necessitating the on-line waveform capabilities of the ventilator. Provided that the ventilator is correctly calibrated and the V'_I is achieved relatively fast (< 0.4 s), the P-T curve may provide all the information obtained by the corresponding P-V curve. Therefore, determination of clinically relevant points obtained by a P-V curve may be obtained using any ventilator without on-line waveform capabilities with a reasonable time delay in achieving constant flow, a disposable pressure transducer and the bedside screen of the patient's monitor. This is an alternative method for determination of the shape of the P-V curve that might be used in intensive care units where, due to limited financial resources, volume recording can not be performed.

References

1. Matamis D, Lemaire F, Harf A, Brun-Buisson C, Ansquer JC, Atlan G (1984) Total respiratory pressure-volume curves in the adult respiratory distress syndrome. Chest 86: 58–66
2. Benito S, Lemaire F (1990) Pulmonary pressure-volume relationship in acute respiratory distress syndrome: role of positive end-expiratory pressure. J Crit Care 1: 27–34
3. Tremblay L, Valenza F, Ribeiro SP, Li J, Slutsky AS (1997) Injurious ventilatory strategies increase cytokines and c-fos m-RNA expression in an isolated rat lung model. J Clin Invest 99: 944–952

4. Muscedere JG, Mullen JB, Gan K, Slutsky AS (1994) Tidal ventilation at low airway pressure can augment lung injury. Am J Respir Crit Care Med 149: 1327–1334
5. Corbridge TC, Wood LD, Crawford GP, Chudoba MJ, Yanos J, Sznajder JI (1990) Adverse effects of large tidal volume and low PEEP in canine acid aspiration. Am Rev Respir Dis 142: 311–315
6. Dreyfuss D, Basset G, Soler P, Saumon G (1985) Intermittent positive-pressure hyperventilation with high inflation pressures produces pulmonary microvascular injury in rats. Am Rev Respir Dis 132: 880–884
7. Chiumello D, Goesev P, Slutsky AS (1999) Mechanical ventilation affects local and systemic cytokines in an animal model of acute respiratory distress syndrome. 160: 109–116
8. Amato MB, Bardas CS, Medeiros DM, Schettino GP, Lorenzi G, Kairalla RA, Deheinzelin D, Moraisz C, Fernandes E de O, Takagaki TY Carvalho CR (1995) Beneficial effects of the open lung approach with low distending pressures in acute respiratory distress syndrome. A prospective randomized study on mechanical ventilation. Am J Respir Crit Care Med 152: 1835–1846
9. Ranieri VM, Suter PM, Tortotella C, De Tullio R, Dayer JM, Brienza A, Bruno F, Slutsky AS (1999) Effects of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA 282: 54–61
10. Slutsky AS, Trembley LN (1998) Multiple system organ failure: is mechanical ventilation a contributing factor? Am J Respir Crit Care Med 157: 1721–1725
11. Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, Takagaki TY, Carvalho CR (1998) Effect of protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 338: 347–354
12. Levy P, Similowski T, Corbeil C, Albala M, Pariente R, Millic Emili J, Jonson B (1989) A method for studying the static volume-pressure curves of the respiratory system during mechanical ventilation. J Crit Care 4: 83–89
13. Gattinoni L, Mascheroni D, Basilico E, Forti G, Pesenti A, Avalli L (1987) Volume-pressure curve of total respiratory system in paralyzed patients: artifacts and corrections factors. Intensive Care Med 13: 19–25
14. Lu Q, Vieira S, Richecoeur J, Puybasset L, Kalfon P, Coriat P, Rouby JJ (1999) A simple automated method for measuring pressure-volume curves during mechanical ventilation. Am J Respir Crit Care Med 159: 275–280
15. Rodriguez L, Marquer B, Mardrus P, Molenat F, Le Grand JL, Reboul M, Carrigues B (1999) A new simple method to perform pressure-volume curves obtained under quasi-static conditions during mechanical ventilation. Intensive Care Med 25: 173–179
16. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson LD, Lamy M, Legall JR, Morris A, Spragg R and the Consensus Committee (1994) American-European consensus conference on ARDS. Am J Respir Crit Care Med 149: 818–824
17. Venegas JG, Harris RS, Simon BA (1998) A comprehensive equation for the pulmonary pressure-volume curve. J Appl Physiol 84: 389–395
18. Harris RS, Hess DR, Venegas JG (2000) An objective analysis of the pressure-volume curve in the adult respiratory distress syndrome. Am J Respir Crit Care Med 161: 432–439
19. Bland J, Altman D (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1: 307–310
20. Murray JF, Matthay MA, Luce JM, Flick MR (1988) An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis 138: 720–723
21. Gottfried SB, Rossi A, Higgs BD, Zocchi L, Grassino A, Milic-Emili J (1985) Respiratory mechanics in mechanically ventilated patients with respiratory failure. J Appl Physiol 58: 1849–1858
22. Mergoni M, Martelli A, Volpi A, Primavera S, Zuccoli P, Rossi A (1997) Impact of positive end-expiratory pressure on chest wall and lung pressure-volume curve in acute respiratory failure. Am J Respir Crit Care Med 156: 846–854
23. Hickling KG (1998) The pressure-volume curve is greatly modified by recruitment. A mathematical model of ARDS lungs. Am Rev Respir Dis 158: 194–202
24. Jonson B, Richard JC, Straus C, Mancebo J, Lemaire F, Brochard L (1999) Pressure-volume curves and compliance in acute lung injury: evidence of recruitment above the lower inflection point. Am J Respir Crit Care Med 159: 1172–1178
25. Dambrosio M, Roupie E, Mollet JJ, Anglade MC, Vasile N, Lemaire F, Brochard L (1997) Effects of positive end-expiratory pressure and different tidal volumes on alveolar recruitment and hyperinflation. Anesthesiology 87: 495–503