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PHYSIOLOGICAL AND TECHNICAL NOTES

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A new automated method versus continuous positive airway pressure method for measuring pressure–volume curves in patients with acute lung injury

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Abstract *Objective:* To compare pressure–volume (*P–V*) curves obtained with the Galileo ventilator with those obtained with the CPAP method in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).
Design: Prospective, observational study. *Setting:* General critical care center. *Patients and participants:* Patients with ALI/ARDS and receiving mechanical ventilation.
Interventions: Pressure–volume curves were obtained in random order with the CPAP technique and with the software PV Tool-2 (Galileo ventilator). *Measurements and results:* In ten consecutive patients, airway pressure was measured by a pressure transducer and changes in lung volume were measured by respiratory inductive plethysmography. *P–V* curves were fitted to a sigmoidal equation with a mean R^2 of 0.994 ± 0.003. Intraclass correlation coefficients were all >0.75 ($P < 0.001$ at all pressure levels). Lower (LIP) and upper inflection (UIP), and deflation maximum curvature (PMC) points calculated from the fitted variables showed a good correlation between methods with intraclass correlation coefficients of 0.98 (0.92, 0.99), 0.92 (0.69, 0.98), and 0.97 (0.86, 0.98), respectively ($P < 0.001$ in all cases). Bias and limits of agreement for LIP (0.51 ± 0.95 cmH_2O; −1.36 to 2.38 cmH_2O), UIP (0.53 ± 1.52 cmH_2O; −2.44 to 3.50 cmH_2O), and PMC (-0.62 ± 0.89 cmH_2O; −2.35 to 1.12 cmH_2O) obtained with the two methods in the same patient were clinically acceptable. No adverse effects were observed.
Conclusion: The PV Tool-2 built into the Galileo ventilator is equivalent to the CPAP method for tracing static *P–V* curves of the respiratory system in critically ill patients receiving mechanical ventilation.

Keywords Acute lung injury · Acute respiratory distress syndrome · Static pressure–volume curves of the respiratory system · Continuous airway positive pressure · Mathematical fitting of respiratory data

Introduction

Pressure–volume (*P–V*) curves analyze static mechanical properties of the respiratory system by relating airway pressure in no-flow conditions with lung volume at the same pressure [1]. Selecting a positive end-expiratory pressure (PEEP) above the lower inflection point (LIP) improves survival in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) [2, 3] and lessens the inflammatory response in ARDS patients [4]. Similarly, airway plateau pressure is a determinant of lung injury in ARDS patients [5]. Therefore, the second point of maximum curvature, the upper inflection point, (UIP) should be the maximum plateau pressure [6]. Moreover, the point of maximum curvature (PMC) on the deflation limb of the curve could be used to adjust PEEP to avoid repeated end-expiratory alveolar collapse [7–9].

We proposed the continuous positive airway pressure (CPAP) method to trace inspiratory and expiratory *P–V* curves. This method is simple, does not require ventilator disconnection, and concorded well with the super-syringe method [10]. The manufacturer Hamilton developed the PV Tool-2 built into the Galileo ventilator (Hamilton Medical) to trace static *P–V* curves of the entire respiratory system. The Galileo ventilator's built-in PV Tool-2 simplifies *P–V* curve tracing and enables physicians without specific training to elaborate *P–V* curves; thus, it is important to know the accuracy of this method before incorporating it into clinical practice. We hypothesized that *P–V* curves traced with the PV Tool-2 method at slow pressure/time ramp (3 cmH_2O/s) would be equivalent to *P–V* curves traced with the static CPAP method in mechanically ventilated patients with ALI/ARDS. Preliminary results of this study have been reported in abstract form [11].

Materials and methods

Patients

Informed, written, next-of-kin consent was obtained for all patients. We enrolled ten consecutive, intubated, mechanically ventilated (Servo Ventilator 900 C, Siemens) patients who met the American-European Consensus Conference criteria for ALI/ARDS [12]. Exclusion criteria were age under 18 years, pregnancy, intracranial hypertension, hemodynamic instability, chest wall abnormalities, or air leaks. Patients were deeply sedated with midazolam and morphine and relaxed with vecuronium bromide if needed [13]. ECG, invasive blood pressure, and pulse oximetry were continuously monitored (Hewlett Packard M1166A). Airway pressure was measured by pressure transducer (MP45, Valydine). End-expiratory lung volume was measured by respiratory inductive plethysmography (RIP) (NIMS) with a thoracic strip. RIP was calibrated by performing a linear procedure that included a first point at functional residual capacity and a second point at the end of inspiration. Once calibrated, RIP measurements were checked by comparing the volume values obtained by RIP and flow integration during tidal ventilation (mean tidal volume, 419 ± 132 mL vs. 444 ± 147 mL measured using RIP and the pneumotachograph, respectively, $R^2 = 0.96$). PEEP was not applied during calibration. A data acquisition system (Windaq 200, Data Q) connected to each monitor allowed analog-to-digital conversion and storage of pressure and RIP signals sampled at 100 Hz. After 10 min baseline ventilation and stabilization, *P–V* curves were traced in random order with the CPAP technique and with the PV Tool-2, separated by a 10-min period to restore baseline conditions.

P–V curves with CPAP technique

After volume history standardization (three 10 ml/kg breaths), the Servo Ventilator 900 C was switched to CPAP mode, a complete exhalation, until expiratory flow reached zero (6–10 s) was performed, and the expiratory volume measured with RIP was recorded. Airway pressure was raised from 0 to 35 cmH_2O in 5 cmH_2O steps. Then, CPAP was decreased from 35 to 0 cmH_2O. At each step, airway pressure and volume were recorded. To ensure static conditions, each change in airway pressure was effected only when flow reached zero.

P–V curves with the PV Tool-2 built into the Galileo ventilator

This method is based on a linear, pressure-controlled ramp, adjustable for ramp speed and maximum pressure. After volume history standardization, we used a pressure ramp of 3 cmH_2O/s and a maximum pressure of 35 cmH_2O. Flow was measured using the ventilator's proximal pneumotachograph (PN279331, Hamilton Medical) inserted between the endotracheal tube and the Y-piece. Volume was obtained from integration of flow. Pressure, flow, and volume data were recorded in a personal computer. At the start of the maneuver, the ventilator performs a prolonged exhalation that lasts for five expiratory time constants to achieve functional residual capacity. In order to study the influence of resistive pressures in the shape of the *P–V* curve, after elaborating the *P–V* curve with the pressure ramp of 3 cmH_2O/s, a new *P–V* curve was traced with pressure ramp of 5 cmH_2O/s in patients 2, 3, 5, 9, and 10 (Table 1).

P–V curves analysis

P–V curves were constructed by plotting airway pressure against RIP volume in the CPAP technique and airway pressure against ventilator-measured volume in the PV Tool-2 technique. As pressure and volume steps differed between methods, pressure–volume data pairs were fitted to a sigmoidal model modified from the equation proposed by Venegas et al. [14], and volumes corresponding to airway pressure of 0–35 cmH_2O in 5 cmH_2O steps were interpolated. The equation is $\mathrm{Vol} = b/\{1 + \mathrm{EXP}[-(\mathrm{Paw} - c)/d]\}$, where Vol is volume, Paw airway pressure, *b* the upper asymptote of the curve, *c* the pressure where curvature changes sign, and *d* the pressure range where most volume change occurs. This model allows objective, reproducible calculation of the inflection points as follows. On the inspiratory limb, LIP was equal

Table 1 Demographics characteristics

Subject number	Sex	Age (years)	Cause of ALI/ARDS	PaO_2/FiO_2 (mmHg)	PEEP (cmH_2O)	Crs (ml/cmH_2O)
1	M	68	Severe sepsis	230	6	36
2	M	79	Pneumonia	143	12	56
3	M	82	Pneumonia	229	8	30
4	M	69	Pneumonia	257	7	38
5	F	66	Septic shock	142	12	42
6	M	72	Brain trauma	270	7	27
7	F	69	Aspirative pneumonia	283	8	31
8	M	69	Peritonitis	125	16	33
9	M	79	Aspirative pneumonia	274	6	42
10	F	76	Severe sepsis	170	12	30

Crs compliance of the respiratory system [Crs = tidal volume/(airway plateau pressure − total PEEP)]

to $c - 1.317d$ and the upper inflection point was equal to $c + 1.317d$. On the deflation limb, PMC was calculated as $c + 1.317d$. These points corresponded to the airway pressure where the *P–V* curve has its maximal upward or downward curvature. Following the same equation makes it possible to calculate the maximal inspiratory and expiratory compliance as: $b/4d$.

Statistical analysis

The model was fitted using nonlinear regression (least squares method). The two methods of measurement were correlated by calculating the bias and limits of agreement (bias ± 1.96 SD) as proposed by Bland and Altman [15]. The intraclass correlation coefficient (ICC) for absolute agreement was calculated for each pressure level. An ICC >0.75 was considered very good agreement [16]. Data are expressed as mean ± SD or median and interquartile range (IQR), except values from the Bland–Altman analysis, which are expressed as mean (95% confidence interval) and limits of agreement. We considered $P < 0.05$ significant. We used SPSS 12.0 (SPSS) for all tests.

Results

Table 1 summarizes patients' characteristics. No deleterious hemodynamic or respiratory effects were identified in any patient. Obtaining the total (inspiratory and expiratory loops) *P–V* curve took 55 ± 6 s with CPAP technique, 34 ± 3 s with the PV Tool-2 pressure ramp of 3 cmH_2O/s and 17 ± 3 s with the PV Tool-2 pressure ramp of 5 cmH_2O/s ($P < 0.01$ for each comparison).

End-expiratory lung volume

End-expiratory lung volume measured before *P–V* curve tracing with each method in each patient was recorded. No significant differences were found (Table 2).

Mathematical fitting of *P–V* curves

All *P–V* curves were fitted to the mathematical model with a mean R^2 of 0.994 ± 0.003. Correlation between curves obtained with the two methods was excellent, and the two curves were almost identical (Fig. 1a). All ICCs were >0.75 ($P < 0.001$) at all pressure levels (Fig. 1a). However, curves obtained with PV tool-2 pressure ramp of 5 cmH_2O/s were different compared with those obtained with pressure ramp of 3 cmH_2O/s and the ICCs were <0.75 (Fig. 1b).

Correlations for inflection points and compliance

LIP, UIP, PMC, and inspiratory and expiratory compliance calculated from the fitted variables showed good correlation between methods, with ICCs of 0.98 (0.92, 0.99); 0.92 (0.69, 0.98); 0.97 (0.86, 0.98); 0.99 (0.97, 0.99), and 0.95 (0.83, 0.98), respectively, ($P < 0.001$) (Table 3). Bias for LIP measurements was 0.51 ± 0.95 cmH_2O and limits of agreement were −1.36 and 2.38 cmH_2O. For UIP measurements, bias was 0.53 ± 1.52 cmH_2O and limits

Table 2 Values of end-expiratory lung volume measured before *P–V* curve tracing with each method in each patient

Patient	preCPAP (mL)	pre PV Tool-2 (mL)
1	369	389
2	599	645
3	254	241
4	312	380
5	317	300
6	287	330
7	587	606
8	582	657
9	435	422
10	450	473
Median	402	405
IQ 25%	313	342
IQ 75%	549	573

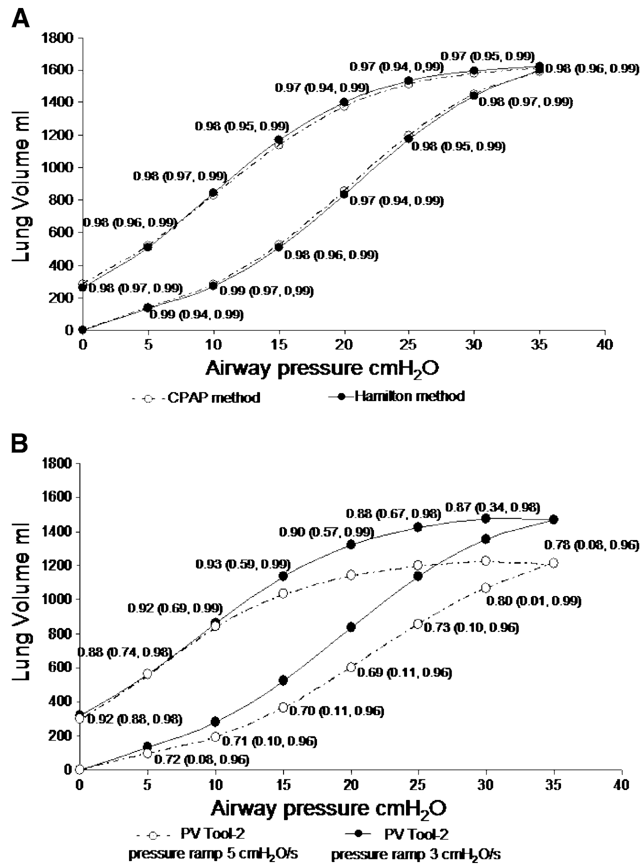

Fig. 1 **a** Pressure–volume curves obtained with the two methods (CPAP method and Hamilton method at 3 cmH_2O/s of pressure/time ramp) in ten patients. Intraclass correlation coefficients (average and 95% CI) for each point are presented. **b** Pressure–volume curves obtained with the PV Tool-2 method, with two different pressure/time ramps: 3 and 5 cmH_2O/s in five patients (patients 2, 3, 5, 9, and 10) Intraclass correlation coefficients (average and 95% CI) for each point are presented

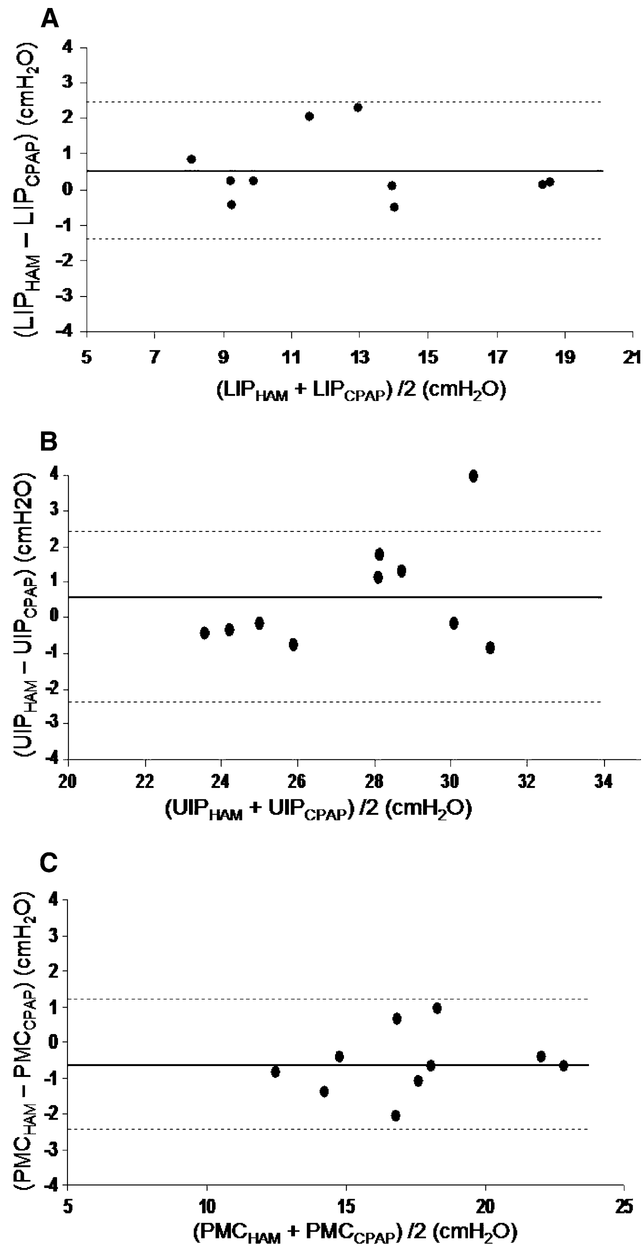

Fig. 2 Concordance analysis plots showing bias (*thick line*) and limits of agreement (*dashed lines*) between the two methods. **a** Plot for LIP (lower inflection point), **b** plot for UIP (upper inflection point), and **c** plot for PMC (point of maximum curvature); *CPAP* continuous positive airway pressure, *HAM* Hamilton

Table 3 Values of lower inflection point (LIP), upper inflection point (UIP), point of maximum curvature (PMC), and inspiratory and expiratory compliance obtained with each *P–V* curve method

	Hamilton method (PV Tool-2)	CPAP method
LIP (cmH_2O)	12.85 ± 3.69	12.34 ± 3.80
UIP (cmH_2O)	27.81 ± 3.12	27.28 ± 2.46
PMC (cmH_2O)	17.09 ± 3.35	17.70 ± 3.17
Inspiratory compliance (mL/cmH_2O)	74.52 ± 39.46	74.70 ± 40.89
Expiratory compliance (mL/cmH_2O)	75.44 ± 43.70	70.39 ± 37.97

of agreement were −2.44 and 3.50 cmH_2O. For PMC measurements, bias was −0.62 ± 0.89 cmH_2O and limits of agreement were −2.35 and 1.12 cmH_2O. Bland–Altman plots for LIP, UIP, and PMC values are represented in Fig. 2a,b, and c, respectively.

Discussion

P–V curves traced with the PV Tool-2 seem equivalent to those obtained with the CPAP technique. However, the PV

Tool-2 method is faster and requires no additional equipment. The super-syringe method (generally considered the gold standard) requires the patient to be disconnected from the ventilator, involving possible adverse effects, and the entire maneuver (inspiratory and expiratory limbs) is time consuming (in some studies longer than 100 s [17], twice as long as the CPAP method). Furthermore, this technique requires additional equipment. Techniques to avoid these drawbacks (multiple occlusions and quasi-static low-flow inflation) usually do not allow tracing of the deflation limb. Moreover, the multiple occlusion technique takes several minutes and PEEP must be set at 0 cmH_2O, so it is cumbersome in clinical practice and can be transiently detrimental [18–21]. The low-flow inflation technique requires considering the resistive pressure component when flow is >9 L/min [1, 19, 20]. Two solutions to obviate the resistive component in quasi-static methods are: subtracting the resistive pressure in tubing and airways from the total pressure [22, 23], and reducing the constant flow [20]. The first requires complex computerized systems [22], and limiting inspiratory airflow to <9 L/min does not allow high tidal volumes in conventional ventilators, making it very difficult to explore the upper part of the *P–V* curve [20]. In the PV Tool-2 method, flow is non-constant in order to achieve a designed pressure/time ramp. Airflow changes during the maneuver in function of the patient's respiratory mechanics. In our study, we calculated the average flow for each curve between 1.5 and 7.7 L/m, all of which were <9 L/min. With this extremely low flow, the resistive pressures can be ignored [1, 20]. To illustrate this point, we performed PV curves using the PV Tool-2 method with two different pressure/time ramps: 3 and 5 cmH_2O/s with the latter ramp average flows in our patients were higher (2.4–18 L/m) and we found a clear shift to the right in the faster curve (Fig. 1b and Figs. 1e–5e in electronic supplementary material).

Critique of the methods

The *P–V* curve obtained with the CPAP technique is time consuming and needs a well-trained clinician because changes in CPAP are difficult (operator-or machine-limited) in some ventilators. Moreover, some conventional ventilators need RIP to measure volume [10], and RIP has limitations to accuracy [24] and requires further analysis for interpretation. Furthermore, the use of a single thoracic band requires muscle paralysis [25].

In contrast, the PV Tool-2 requires no special learning. The complete *P–V* curve can be traced in less than 35 s without ventilator disconnection and results are immediate. Inflation and deflation limbs can be obtained, and minimal PEEP can be used to avoid lung derecruitment. *P–V* curve repeatability with both methods was not assessed because alveolar recruitment and derecruitment phenomena inherent to each *P–V* curve maneuver would make data difficult to interpret.

Finally, a limitation of the Galileo ventilator's built-in PV Tool-2 is that the inflection points must be determined by eye fitting or by exporting the data. This makes a "well-trained physician" necessary, just like in the CPAP method.

Conclusions

The PV Tool-2 built into the Galileo ventilator is a valid alternative for bedside total respiratory system *P–V* curve tracing. Moreover, drawbacks inherent in other techniques are avoided. The technique is simple and needs no additional equipment or specialized learning.

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