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Volumetric capnography in patients with acute lung injury: effects of positive end-expiratory pressure

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Volumetric capnography in patients with acute lung injury: effects of positive end-expiratory pressure. Ll. Blanch, U. Lucangelo, J. Lopez-Aguilar, R. Fernandez, P.V. Romero. ©ERS Journals Ltd 1999.

ABSTRACT: The aim of the study was to analyse the effects of positive end-expiratory pressure (PEEP) on volumetric capnography and respiratory system mechanics in mechanically ventilated patients.

Eight normal subjects (control group), nine patients with moderate acute lung injury (ALI group) and eight patients with acute respiratory distress syndrome (ARDS group) were studied. Respiratory system mechanics, alveolar ejection volume as a fraction of tidal volume (V_{AE}/V_T), phase III slopes of expired CO_2 beyond V_{AE} and Bohr's dead space (V_D/V_T(Bohr)) at different levels of PEEP were measured.

No differences in respiratory system resistances were found between the ALI and ARDS groups. V_D/V_T(Bohr) and expired CO_2 slope beyond V_{AE} were higher in ALI patients (0.52±0.01 and 13.9±0.7 mmHg·L^{-1}, respectively) compared with control patients (0.46±0.01 and 7.7±0.4 mmHg·L^{-1}, p<0.01, respectively) and in ARDS patients (0.61±0.02 and 24.9±1.6 mmHg·L^{-1}, p<0.01, respectively) compared with ALI patients. V_{AE}/V_T differed similarly (0.6±0.01 in control group, 0.43±0.01 in ALI group and 0.31±0.01 in ARDS group, p<0.01). PEEP had no effect on V_{AE}/V_T, expired CO_2 slope beyond V_{AE} and V_D/V_T(Bohr) in any group. A significant correlation (p<0.01) was found between V_{AE}/V_T and expired CO_2 slope beyond V_{AE} and lung injury score at zero PEEP.

Indices of volumetric capnography are affected by the severity of the lung injury, but are unmodified by the application of positive end-expiratory pressure.
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Acute respiratory failure severely alters respiratory system mechanics. Most of these changes affect peripheral structures beyond the conducting airways: *i.e.* the interstitium, alveolar spaces, and small airways. The main consequence of the peripheral lung injury is the development of heterogeneities that affect the efficacy of respiratory gas exchange and ventilatory distribution. Assessment of respiratory mechanics is currently performed by the measurement of respiratory system compliance (C_{rs}) and total respiratory system resistance (R_{rs}) [1–3]. The constant flow interrupter technique allows the separation of the two main components of R_{rs}: the first related to airways resistance and to the Newtonian component of chest wall dynamics (R_{min}), and the second, called differential resistance (R_{diff}), related to the rheological properties of the respiratory tissues and to the pendelluft effect. Previous studies have shown that all of these mechanical parameters are altered in the acute respiratory distress syndrome (ARDS) [4–6].

Ventilatory heterogeneity can also be assessed by volumetric capnography, a technique that analyses the pattern of CO_2 elimination as a function of expired volume. Volumetric capnograms, already used to monitor alveolar ventilation [7–9], reveal steeper phase III slopes in patients with airways obstruction [10–12], and are helpful to assess ventilatory maldistribution in critically ill patients [13–15].

Positive end-expiratory pressure (PEEP) is commonly applied to improve gas exchange in patients with ARDS, although changes in respiratory mechanics after the application of PEEP are not completely understood. Several studies have shown that R_{diff} increases at high PEEP levels, suggesting that PEEP may either change the viscoelastic properties of the lung by overdistending previously aerated lung regions of increasing lung heterogeneity and the pendelluft effect or both [2, 4, 6]. Currently, the effects of different levels of PEEP on volumetric capnography in patients with varying degrees of acute lung injury (ALI) are unknown. Therefore, the objective of this investigation was to analyse the effects of PEEP on computerized volumetric capnography and respiratory system mechanics in mechanically ventilated patients with varying degrees of lung injury.

Materials and methods

Study subjects

This study was performed in the Hospital of Sabadell according to the principles established in Helsinki and with

the approval of the Ethics Committee for Clinical Investigations. Informed consent was obtained from control subjects and from the patients' closest relatives prior to the study. During the experiments, another physician not involved in the protocol was always present to provide patient care.

Control subjects. Eight normal subjects receiving total intravenous anaesthesia and scheduled for elective minor surgery were studied before the surgical intervention. All subjects were nonsmokers, none were obese or had any evidence of cardiopulmonary disease or a history of chronic lung disease, and their respiratory function had been classified as normal by the preoperative evaluation of the anaesthesiologist. Total intravenous anaesthesia was induced with propofol (2–2.5 mg·kg of body weight^{-1}) and muscle relaxation was induced with atracurium besilate (0.5–0.6 mg·kg^{-1}). Subjects were transorally intubated with a cuffed endotracheal tube (Hi-lo Evac; Mallinckrodt Lab., Athlone, Ireland) (ID 7.5–8.5 mm). Anaesthesia and paralysis were maintained by continuous infusions of propofol (4–12 mg·kg^{-1}·h^{-1}), fentanyl (3 μg·kg^{-1}·h^{-1}) and atracurium besilate (0.3–0.6 mg·kg^{-1}·h^{-1}). Subjects were mechanically ventilated (Servo 900C; Siemens, Solna, Sweden) in assist/control mode with a square-wave flow profile. Ventilatory pattern and inspiratory oxygen fraction (F_{I,O_2}) were set to maintain end-tidal carbon dioxide tension (P_{ET,CO_2}) and haemoglobin oxygen saturation (measured by pulse oximetry) within a range of 4.0–4.5 kPa (30–34 mmHg) and 97–100%, respectively.

Acute lung injury patients. Nine patients with moderate ALI admitted to the general Intensive Care Service were studied within the first 48 h of mechanical ventilation. ALI was defined according to the American–European Consensus Conference [16]. Lung injury score (LIS) was calculated in all patients [17]. LIS ranged 0.50–2.25, indicating mild-to-moderate ALI. Patients with a previous history of obstructive airway disease and chest wall abnormalities (flail chest or pneumothorax) and/or evidence of heart failure were excluded. Patients were sedated intravenously with midazolam (0.2 mg·kg^{-1}) and paralysed with atracurium besilate (0.5–0.6 mg·kg^{-1}). Patients were transorally intubated with a cuffed endotracheal tube (Hi-lo Evac; Mallinckrodt Lab.) (ID 8–8.5 mm) and mechanically ventilated (Servo 900C) in assist/control mode with a square-wave flow profile. Heart rate, electrocardiogram, invasive systemic arterial pressure and continuous noninvasive assessment of oxygen saturation with pulse oximetry were monitored in all patients. At the time of the study all patients were in a stable clinical condition.

Acute respiratory distress syndrome patients. Eight patients diagnosed with ARDS were studied within the first 72 h of mechanical ventilation. ARDS was defined according to the American–European Consensus Conference [16]. LIS was calculated in all patients [17]. LIS ranged 2.75–3.75 indicating ARDS. Exclusion criteria, sedation and paralysis, breathing pattern on mechanical ventilation and monitoring were the same as those described for the ALI group. At the time of the study all patients were in a stable clinical condition.

Study design

Physiological measurements were performed at four levels of PEEP (0, 5, 10 and 15 cmH_2O) applied in random order while other ventilatory parameters were kept constant. Each PEEP stage was preceded by aspiration of pulmonary secretions and a sequence of three volume sighs to standardize lung volume history. Measurements were obtained under steady-state conditions after a minimum of 10 min without any observed variation in pulse oximetry and in P_{ET,CO_2} readings. Infusion rates of fluids and vasoactive drugs were kept constant throughout the study.

Methods

Airway opening pressure was measured *via* a T-piece proximal to the endotracheal tube. Tracheal pressure (P_{tr}) was measured using a noncompliant polyethylene catheter (length 50 cm; ID 1.5 mm) with distal multiple sideholes connected to a pressure transducer (MicroSwitch; Honeywell Ltd., Scarborough, Ontario, Canada). The tracheal catheter was placed 1.5–2 cm past the distal end of the endotracheal tube. The frequency response of the catheter was tested and was linear up to 20 Hz. Airflow ($\dot{V}$) was measured using a heated Fleisch no. 2 pneumotachograph (Metabo, Epalinges, Switzerland) placed between the endotracheal tube and the Y-connector of the ventilator. The response of the pneumotachograph was linear over the experimental flow range. Tidal volume (V_T) was obtained by integrating the expiratory flow signal over expiratory time. To minimize the effects of ventilator tubing compliance on volume measurements, low-compliance tubing (0.4 mL·cmH_2O^{-1}) without a heat and moisture exchanger was used. Expiratory carbon dioxide tension (P_{CO_2}) was recorded by means of a capnograph ($CO_2/F_{I,O_2}$ Module HP78556A; Hewlett Packard, Palo Alto, CA, USA) positioned between the pneumotachograph and the endotracheal tube. Total instrumental dead space was 80 mL. The delay of the capnometer was 180 ms, and it was individually assessed and corrected in each patient. The individual patient delay was computed as the time elapsed between the beginning of the inspiration assessed by capnography (rapid drop of CO_2 after phase III) and the beginning of inspiration detected by the pneumotachograph. Before each study, the CO_2 analyser was calibrated using a certified gas with a known concentration of CO_2.

Signals were amplified and filtered at a corner frequency of 100 Hz (ECLER 8-poles Bessel filter, Barcelona, Spain) sampled at 250 Hz by means of an analogue-to-digital converter (DT-2801A; Data Translation, Marlboro, MA, USA) and stored in magnetic media for off-line processing.

Respiratory system mechanics were assessed by end-inspiratory and end-expiratory occlusion techniques during constant-flow volume-cycled ventilation [1]. The end-inspiratory occlusion manoeuvre lasted 4 s. After occlusion, maximal tracheal pressure ($P_{tr,max}$) dropped to the pressure occurring after closure of the ventilator valve (P_1) and then gradually decayed from P_1 to an apparent plateau that represents the end-inspiratory static recoil pressure of the total respiratory system (P_{el}). Methodological problems in calculating real values of $P_{tr,max}$ and pressure at zero flow conditions (P_1) were solved as described [18, 19]. Briefly, $P_{tr,max}$ was corrected for the volume change

during closure of the inspiratory valve. Volume change during valve closure was calculated as the difference between the inspired volume corresponding to the last constant inspiratory flow condition (valve completely open) and to that corresponding to the first point where the inspired volume became constant. The latter point coincides with a 50% reduction in valve conductance (personal observation) beyond which volume change is negligible. By using a dynamic pressure–volume curve, the $P_{tr,max}$ increment due to volume change during valve closure can be estimated by forward extrapolation of P_{tr}. P_1 was obtained by fitting P_{tr} to a fourth degree polynomial and then back extrapolating to the time of 50% valve closure. Auto or intrinsic PEEP were measured by isolating the respiratory system at end-expiration (*via* the end-expiratory hold button of the ventilator) until P_{tr} reached a plateau (usually in 3s).

Total PEEP defined as the sum of PEEP and auto-PEEP was measured at the tracheal level. Static compliance of the respiratory system ($C_{rs,st}$) was computed by: $V_T/(P_{el}$ - total PEEP). Endotracheal tube resistance was computed by dividing peak airway opening pressure minus $P_{tr,max}$ by inspiratory airflow (V'_I). R_{rs} was calculated as the total drop in P_{tr} ($P_{tr,max}$ - P_{el}) divided by V'_I. Airway resistance was calculated as the initial drop in P_{tr} ($P_{tr,max}$ - P_1) divided by V'_I. R_{diff} was obtained by subtracting R_{min} from R_{rs}.

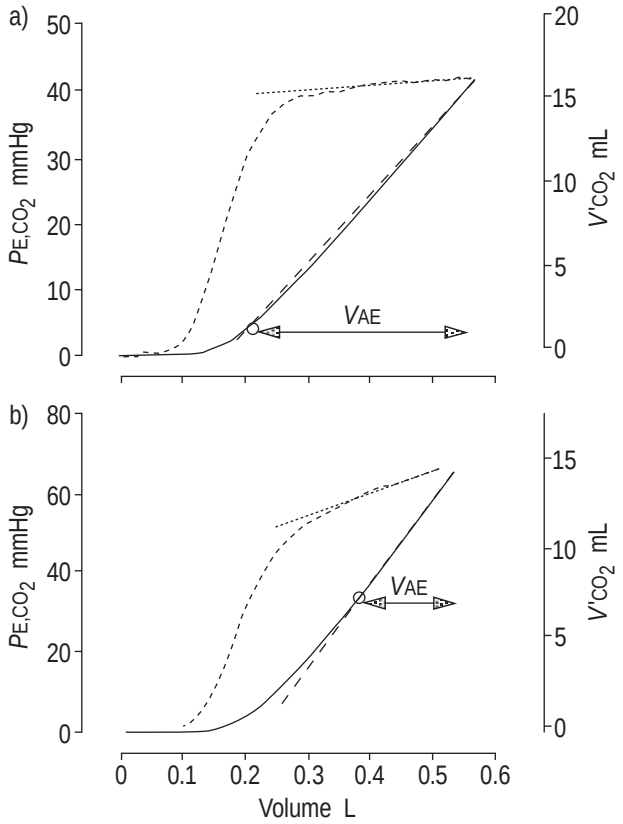

Fig. 1. – Tracings of expiratory carbon dioxide tension (P_{E,CO_2}; - - - -) and instantaneous carbon dioxide production (V'_{CO_2}; ——) as a function of expired tidal volume (V_T) obtained in a normal subject (a) and in an acute respiratory distress syndrome patient (b). Measurements of alveolar ejection volume (V_{AE}) as a function of expired V_T and phase III expired CO_2 slope beyond V_{AE} (·····) are shown. ○: the point at which the V_{T,CO_2}–volume curve intersects a straight line having a maximal value at end expiration with a slope equal to 0.95-times the fitted slope. For further explanation see text.

The expiratory portions of volume and P_{CO_2} signals were isolated using the flow signal as a reference. Instantaneous CO_2 elimination for each tidal breath (V_{T,CO_2}) was obtained by digital integration of P_{CO_2} over the expired V_T. Capnographic indices were measured from the expired P_{CO_2}–volume curve as previously described [15, 20].

Bohr's dead space (V_D/V_T(Bohr)) was calculated from the Bohr equation [7]:

$$V_D/V_T(\text{Bohr}) = (P_{ET,CO_2} - P_{E,CO_2})/P_{ET,CO_2}$$

where P_{E,CO_2} is the mean expiratory carbon dioxide tension calculated from:

$$P_{E,CO_2} = \text{total } V_{T,CO_2}/V_T$$

Alveolar ejection volume (V_{AE}) was determined from V_{T,CO_2} as a function of expired V_T as previously described [15]. Briefly, the slope of the last 50 points of every cycle was obtained by a least-squares linear regression analysis. V_{AE} is the volume exhaled from the point at which the V_{T,CO_2}–volume curve intersects a straight line having a maximal value at end expiration with a slope equal to 0.95-times the fitted slope [21]. V_{AE} is then expressed as a fraction of V_T (V_{AE}/V_T) (fig. 1).

Phase III slopes of expired CO_2 curves were quantified by first defining this phase as the part of the slope corresponding to alveolar air. Theoretically, this occurs during the exhalation of alveolar volume. Therefore, phase III slopes were determined from least-squares linear regression of the linear part of the expired P_{CO_2} curve beyond alveolar air, *i.e.*, beyond V_{AE} (fig. 1).

Analysis

Values are expressed as mean±SEM. One-way analysis of variance (ANOVA) with the Tukey test for multiple comparisons was used to compare mean values obtained at different levels of PEEP in each group. The same method was used to compare mean values obtained in the three groups for each level of PEEP. Multivariate analysis of variance (MANOVA) was used to simultaneously assess the effects of group, level of PEEP and group–PEEP

Table 1. – Clinical data and ventilatory parameters at zero positive end-expiratory pressure (PEEP) in control, acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) patients

	Control n=8	ALI n=9	ARDS n=8
Age yrs	24±4	54±4	57±7
LIS	0.3±0.1	0.9±0.2	2.9±0.1
RR breaths·min^{-1}	13±0.2	18±0.8	23±1.2
V_T L	0.51±0.05	0.53±0.01	0.50±0.02
Airflow L·s^{-1}	0.72±0.01	0.69±0.01	0.75±0.04
AutoPEEP cmH_2O	0	1.5±0.4	3.9±1.3
$P_{a,O_2}/F_{I,O_2}$ mmHg	-	249±21	134±19
P_{a,CO_2} mmHg	-	35±2	46±3

Values are expressed as mean±SEM. LIS: lung injury score; RR: respiratory rate; V_T: tidal volume; P_{a,O_2}: arterial oxygen tension; F_{I,O_2}: inspiratory oxygen fraction; P_{a,CO_2}: arterial carbon dioxide tension. 0.133 kPa=1 mmHg.

Table 2. – Respiratory system mechanics at different positive end-expiratory pressure (PEEP) levels in control, acute lung injury (ALI) and distress syndrome (ARDS) patients

	PEEP cmH_2O			
	0	5	10	15
$C_{rs,st}$ $mL \cdot cmH_2O^{-1}$ $^{\$}$*				
Control‡†	52.7±2.1	61.7±2.1	70.2±4.2§	70.0±4.5§
ALI‡	46.7±5.0	49.3±4.3	47.8±4.0	44.6±3.4
ARDS	38.3±3.0	38.1±3.0	36.0±2.9	32.0±2.7
R_{rs} $cmH_2O \cdot L^{-1} \cdot s$*				
Control‡†	4.0±0.5	3.7±0.4	3.6±0.2	3.7±0.3
ALI	9.5±1.0	8.9±0.8	9.2±1.1	10.1±1.0
ARDS	11.1±0.6	10.2±0.7	10.8±0.6	12.2±1.1
R_{min} $cmH_2O \cdot L^{-1} \cdot s$ $^{\$}$*				
Control‡†	1.9±0.3	1.6±0.3	1.2±0.1	1.2±0.1
ALI	4.9±0.7	4.6±0.6	3.9±0.6	3.6±0.5
ARDS	6.2±0.6	5.2±0.6	4.5±0.7	3.8±0.5
R_{diff} $cmH_2O \cdot L^{-1} \cdot s$ $^{\$}$*				
Control‡†	2.1±0.2	2.1±0.2	2.4±0.1	2.6±0.3
ALI	4.6±0.4	4.3±0.3	5.3±0.5	6.5±0.7$^{\#}$
ARDS	4.8±0.5	5.0±0.5	6.3±0.8	8.5±1.3$^{\S\#}$

Values are expressed as mean±SEM. $C_{rs,st}$: static compliance of respiratory system; R_{rs}: total respiratory system resistance; R_{min}: a component of R_{rs} related to airways resistance and the Newtonian component of chest wall dynamics; R_{diff}: differential resistance, related to the rheological properties of respiratory tissues and the pendelluft effect. $^{\$}$: significant interaction (group and PEEP); *: significantly different between PEEP levels; †: significantly different from the ALI group; ‡: significantly different from the ARDS group; §: significantly different from the value at PEEP 0 cmH_2O; $^{\#}$: significantly different from the value at PEEP 5 cmH_2O.

interaction on the mean values. Significance was taken at $p<0.05$. Associations among variables were analysed using the Pearson correlation coefficient with two-tailed significance taken at $\alpha=0.05$.

Results

Demographic data and ventilatory parameters are depicted in table 1. The underlying disease was medical in six patients and surgical in three patients in the ALI group. The underlying disease was medical in five patients and surgical in three patients in the ARDS group. V' and V_T were similar in all groups. Respiratory rate was higher in ALI and ARDS patients compared with the control group, and in ARDS patients compared to the ALI group. Auto-PEEP was only present in the ALI and ARDS groups.

Respiratory system mechanics are shown in table 2. Static compliance in the ARDS group was significantly lower than in the control ($p<0.01$) and ALI ($p<0.01$) groups. Static compliance response to PEEP was significantly different between the groups (interaction, $p<0.01$). Static compliance did not change in the ALI and ARDS groups, whereas it increased significantly at PEEP 10 and 15 cmH_2O in the control group ($p<0.01$). Endotracheal tube resistance (including the internal catheter) was 9.08±0.8 $cmH_2O \cdot L^{-1} \cdot s$ in control subjects, 8.53±0.82 $cmH_2O \cdot L^{-1} \cdot s$ in ALI patients and 7.94±0.8 $cmH_2O \cdot L^{-1} \cdot s$ in the ARDS group at PEEP 0 cmH_2O and no differences were observed at the different PEEP levels tested in each group. R_{rs} was higher in ALI ($p<0.01$) and ARDS ($p<0.01$) patients compared to control patients. Both R_{min} and R_{diff} exhibited significant interaction between the group and PEEP level ($p<0.01$). Airway resistance and R_{diff}

Table 3. – Volumetric capnographic indices at different postive end-expiratory pressure (PEEP) levels in control acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) patients

	PEEP cmH_2O			
	0	5	10	15
V_D/V_T(Bohr)				
Control‡†	0.46±0.01	0.48±0.01	0.50±0.01	0.49±0.02
ALI‡	0.52±0.01	0.53±0.01	0.54±0.01	0.55±0.01
ARDS	0.61±0.02	0.61±0.02	0.63±0.02	0.65±0.02
Expired CO_2 slope beyond V_{AE} $mmHg \cdot L^{-1}$				
Control‡†	7.7±0.4	6.2±0.5	6.5±0.3	7.4±0.3
ALI‡	13.9±0.7	13.3±0.8	12.6±0.8	12.6±0.8
ARDS	24.9±1.6	26.1±2.2	28.6±2.3	27.9±2.0
V_{AE}/V_T				
Control‡†	0.60±0.01	0.61±0.01	0.60±0.01	0.59±0.01
ALI‡	0.43±0.01	0.45±0.01	0.45±0.01	0.45±0.01
ARDS	0.31±0.01	0.33±0.01	0.31±0.01	0.30±0.01

Values are expressed as mean±SEM. V_D/V_T(Bohr): Bohr's dead space; V_{AE}: alveolar ejection volume; V_T: tidal volume. †: significantly different from the ALI group; ‡: significantly different from the ARDS group.

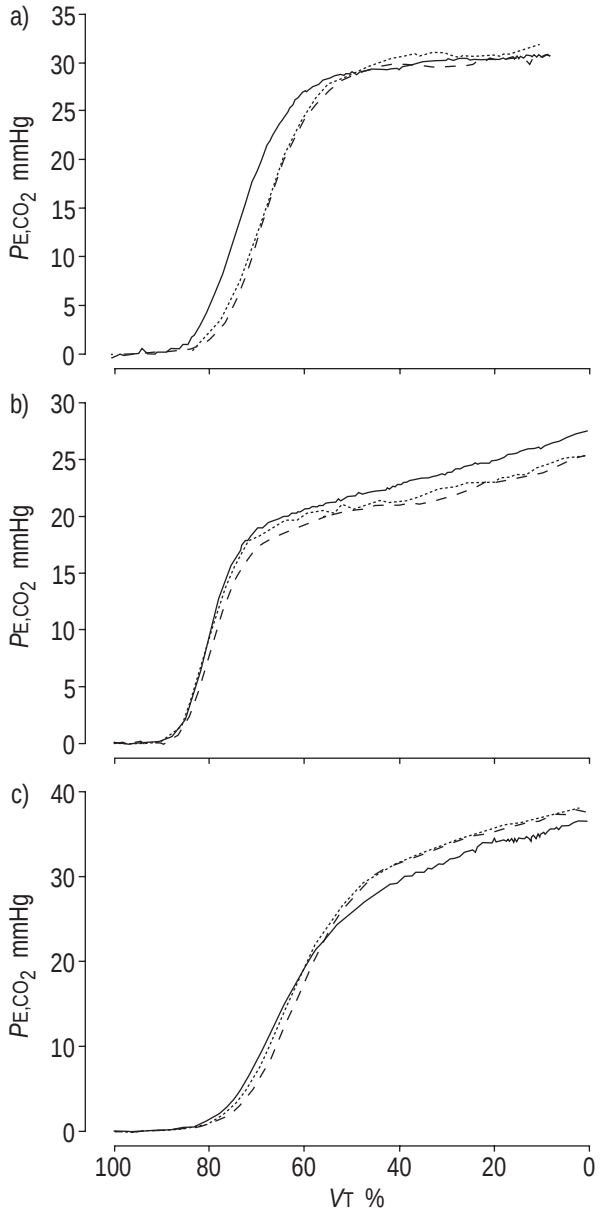

Fig. 2. – Tracings of expiratory carbon dioxide tension (P_{E,CO_2}) as a function of expired tidal volume (V_T, %) obtained in representative patients at different positive end-expiratory pressure (PEEP) levels for a) a normal subject; b) an acute lung injury patient; and c) an acute respiratory distress syndrome patient. —— : PEEP cmH_2O; - - - - : PEEP 10 cmH_2O; – – – : PEEP 15 cmH_2O. Values at PEEP 5 cmH_2O are omitted for clarity.

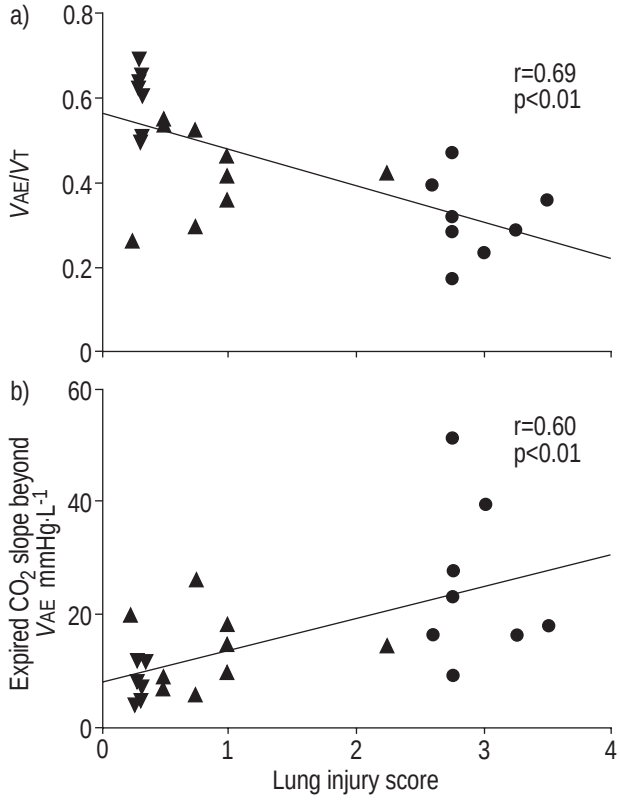

Fig. 3. – Relationships between indices of volumetric capnography (alveolar ejection volume (V_{AE})/tidal volume (V_T) (a) and phase III expired CO_2 slope beyond V_{AE} (b)), and lung injury score at zero end-expiratory pressure in the different groups. ▼: control subjects; ▲: acute lung injury patients; ●: acute respiratory distress syndrome patients.

were lower in control patients compared to ALI ($p<0.01$) and ARDS ($p<0.01$) patients. No differences in R_{rs}, R_{min} and R_{diff} were observed between the ALI and ARDS groups. Additional resistance increased significantly at PEEP 15 cmH_2O in the ALI and ARDS groups ($p<0.05$). In all groups, PEEP had no effect on R_{rs}, and R_{min} showed a tendency to decrease at high PEEP levels.

Indices obtained from volumetric capnography (V_D/V_T (Bohr), and expired CO_2 slope beyond V_{AE} and V_{AE}/V_T) were markedly different among the different groups (table 3). Bohr's dead space and expired CO_2 slope beyond V_{AE} were significantly higher in the ALI group compared to the control group ($p<0.01$), and in the ARDS group when compared to the control ($p<0.01$) and ALI ($p<0.01$) groups. The fraction of V_T corresponding to alveolar volume was significantly lower in the ALI group than in the control group ($p<0.01$), and in the ARDS group compared to the control ($p<0.01$) and ALI ($p<0.01$) groups. In all groups, PEEP had no effect on capnographic indices (table 3, fig. 2). LIS correlated significantly with V_{AE}/V_T and expired CO_2 slope beyond V_{AE} at zero PEEP (fig. 3).

Discussion

The results of this study demonstrate that the severity of the disease affects volumetric capnographic indices and the mechanical properties of the respiratory system. Increasing PEEP improved C_{rs} in normal subjects and increased R_{diff} in patients with respiratory failure, but did not affect volumetric capnographic indices.

Capnography permits recognition of CO_2 concentration changes in the patient's airway during the respiratory cycle. Reliable capnographic measurements require correction of the capnographic signal for the signal delay of the capnometer in order to avoid an important source of error in the measurements. The capnogram represents the total amount of CO_2 eliminated by the lungs. Expired gas receives CO_2 from three sequential compartments forming three recognizable phases on the expired capnogram. Phase I contains gas from apparatus dead space and proximal

conducting airways. Phase II is a transitional region characterized by an increasing CO_2 concentration resulting from progressive CO_2 emptying from alveoli to airways and phase III represents essentially alveolar gas and is known as the alveolar plateau [7, 15, 20]. Very high instrumental resistance might influence capnographic indices but when instrumental resistance does not vary with interventions (such as the behaviour of endotracheal tube resistance with PEEP in this study), variations in phase III of the expired capnogram reflect abnormalities in lung function, and errors, if any, are systematic. Other calculations obtained from volumetric capnograms are V_{T,CO_2} per breath and the airway dead space determined by the vol-ume intercept of a linear regression performed on the V_{T,CO_2}–volume plot [22–24]. For conditions of alveolar nonhomogeneity, the capnographic index V_{AE}/V_T obviates geometrical calculations and nonlinearities of the V_{T,CO_2}–volume plot [15]. As long as the expired volume of gas coming from the alveoli is large enough to wash out airway dead space well before the end of expiration, V_{AE} represents nonsynchronous emptying of the alveoli with unequal ventilation/perfusion ratios. Accordingly, V_D/V_T (Bohr), which is composed of airway dead space plus the part of the alveolar dead space that relies on a sloping alveolar plateau [7], is an index that reflects the emptying characteristics of different alveoli, and V_{AE}/V_T is an index of uneven ventilation/perfusion of heterogeneous alveoli which may be useful to monitor in patients with ARDS receiving mechanical ventilation.

With the exception of patients with airflow obstruction [10–12], there are no data in the literature that evaluate the shape of the capnogram in patients with respiratory failure. In this investigation, the author's preliminary data that capnographic shape is altered in ARDS and ALI patients was confirmed [15]. Moreover, the application of PEEP, an intervention that increases lung volume and alters respiratory system mechanics, did not affect the expired CO_2 slope beyond V_{AE} and V_{AE}/V_T. Two physiological explanations could be considered to analyse these results.

Firstly, the shape of the expired capnogram depends on the homogeneity of the gas distribution and alveolar ventilation [22, 23, 25]. Lung heterogeneity creates regional differences in CO_2 concentration, and gas from high ventilation/perfusion regions first appears in the upper airways during exhalation. This sequential emptying contributes to the rise of the alveolar plateau [22, 26]; the greater the ventilation/perfusion heterogeneity, the steeper the expired CO_2 slope. Accordingly, the slope of the alveolar plateau correlated with spirometry in asthma [11]. Secondly, morphometric increases (lung growth) in the alveolated airway cross-section are associated with a decrease of the expired CO_2 phase III slope [24]. The opposite occurs in emphysema in which a decrease in the alveolated airway cross-section is a characteristic feature [27]. Data on volumetric capnography obtained in the present study are consistent with the physiological concept of nonsynchronous emptying and ventilation/perfusion differences among different lung regions. The observation that both the expired CO_2 slope beyond V_{AE} and V_{AE}/V_T were associated with LIS at zero PEEP is in favour of this hypothesis. However, accurate predictions cannot be calculated from the correlation found between these variables.

The effect of PEEP on volumetric capnography has not been previously evaluated in humans with ARDS. Breen and Mazumdar [28] found that the application of 11 cmH_2O of PEEP in anaesthetized mechanically ventilated open-chested dogs increased physiological dead space, reduced V_{T,CO_2} and resulted in a poorly defined alveolar plateau. These changes were mainly produced by a significant decrease in cardiac output due to PEEP. Although cardiac effects of PEEP were not measured in the present investigation, V_D/V_T(Bohr) did not change significantly with PEEP. Since, P_{ET,CO_2} and mean P_{CO_2} could be influenced by variations in cardiac output [29], a haemodynamic effect of PEEP on these capnographic measurements can reasonably be rejected.

Studies using computed tomographic scans showed that PEEP overdistended previously inflated lung units [30], supporting the concept that high PEEP changes the viscoelastic properties of lung tissues [2, 31]. No modifications in the studied capnographic indices were shown at different PEEP levels in any group. These findings suggest that high PEEP in ARDS and ALI mostly increases stress relaxation and viscoelastic phenomena (increase in R_{diff} at PEEP 15 cmH_2O in the ALI and ARDS groups). However, capnography reflects both variations in ventilation and in perfusion distribution, it being difficult to discriminate between viscoelastic behaviour or pendelluft for the same increase in additional resistance with PEEP.

C_{rs} increased with PEEP only in normal subjects. This observation is in agreement with earlier observations in anaesthetized humans [32], suggesting that airway closure appears at a reduced functional residual capacity in anaesthetized supine normal patients. This explanation is supported by computed tomography studies showing lung collapse in dependent lung zones [33], which completely re-expand after PEEP therapy. The fact that volumetric capnographic indices remained unaltered after PEEP therapy suggests that volumetric capnographic indices reflect alterations only of the ventilated lung areas.

In conclusion, it has been shown that in mechanically ventilated patients, there is a relationship at zero positive end-expiratory pressure between lung injury score and indices derived from volumetric capnography, such as the expired CO_2 slope beyond alveolar ejection volume and alveolar ejection volume as a fraction of tidal volume, and application of positive end-expiratory pressure did not alter volumetric capnographic indices but significantly increased additional respiratory system resistance. These findings indicate that indices derived from volumetric capnography might be useful to assess the severity of the respiratory failure.

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