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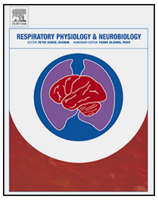

Simultaneous monitoring of intratidal compliance and resistance in mechanically ventilated piglets: A feasibility study in two different study groups

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ABSTRACT

Compliance measures the force counteracting parenchymal lung distension. In mechanical ventilation, intratidal compliance–volume ($C(V)$)-profiles therefore change depending on PEEP, tidal volume (V_T), and underlying mechanical lung properties. Resistance counteracts gas flow through the airways. Due to anatomical linking between parenchyma and airways, intratidal resistance–volume ($R(V)$)-profiles are hypothesised to change in a non-linear way as well. We analysed respiratory system mechanics in fifteen piglets with lavage-induced lung injury and nine healthy piglets ventilated at different PEEP/V_T-settings. In healthy lungs, $R(V)$-profiles remained mostly constant and linear at all PEEP-settings whereas the shape of the $C(V)$-profiles showed an increase toward a maximum followed by a decrease (small PEEP) or volume-dependent decrease (large PEEP). In the lavage group, a large drop in resistance at small volumes and slow decrease toward larger volumes was found for small PEEP/V_T-settings where $C(V)$-profiles revealed a volume-dependent increase (small PEEP) or a decrease (large PEEP and large V_T). $R(V)$-profiles depend characteristically on PEEP, V_T, and possibly whether lungs are healthy or not. Curved $R(V)$-profiles might indicate pathological changes in the underlying mechanical lung properties and/or might be a sign of derecruitment.

1. Introduction

The continuous volume change during tidal breathing induces a continuous impedance change with its two main components airflow resistance and volume distensibility i.e. compliance. The key component of airways' mechanical impedance is resistance (R) counteracting gas flow, the key component of the parenchyma, i.e. alveoli and terminal airways, is compliance (C) counteracting distension. It has been shown that the shape of the intratidal compliance–volume ($C(V)$)-profile indicates indirectly if the lung is ventilated at high or low intrapulmonary volume (Mols et al., 1999, 2006) and could therefore be used to adjust PEEP and tidal volume (V_T) (Schumann et al., 2009). There seems to be a complex relationship between airway calibre, respiratory parenchyma mechanics, and PEEP-setting (Babik et al., 2012) and anatomical linking of parenchyma and airways leads to a mutual influence of their biomechanical behaviour (Pare and Mitzner, 2012). Constriction of airways stiffens the parenchyma and could therefore reduce compliance (Mitzner et al., 1992). Any increase in lung volume, by contrast, tethers open adjacent airways, increases their volume until the basal airway membrane limits further volume increment and, hence, decreases flow-related airway resistance. The intratidal configuration and volume of airways and parenchyma change rhythmically. It can therefore be assumed that the intratidal resistance of the respiratory system also changes depending on ventilation setting (Mols et al., 2001) and underlying mechanical lung properties. Analyses of single points within the breathing cycle (inspiratory peak, inspiratory pause or end-expiratory pressure point) provide a representation of the lung under minimal or no-flow conditions (Hickling, 1998; Jonson et al., 1999). By its very nature, describing the continuously changing conditions

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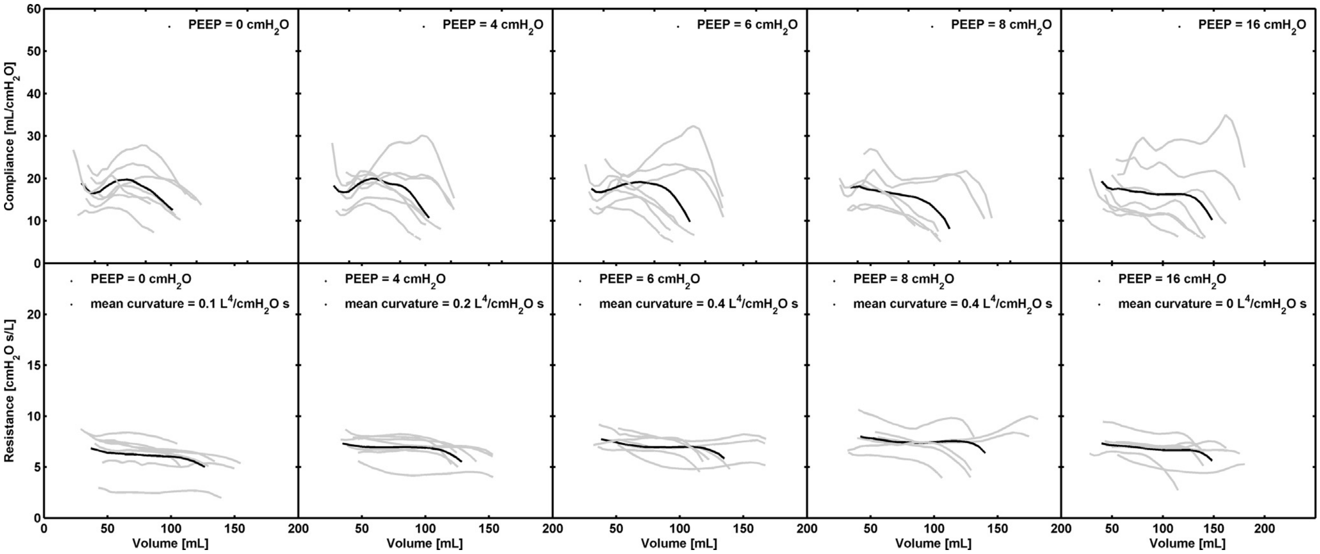

Fig. 1. Top: compliance–volume profiles for lung healthy animals at PEEP-levels of 0, 4, 6, 8, and, 16 cmH_2O and constant tidal volumes. Each grey line represents the average over at least 10 breaths for each single animal. The black lines show the average over all animals. Bottom: same as above but for the resistance–volume profiles. Mean curvature between a 60 and 200 mL volume range are reported in each panel.

of the lung during ongoing mechanical ventilation can only be achieved by mapping the intratidal, non-linear course of R and C (Lichtwarck-Aschoff et al., 2000; Stahl et al., 2006). We use our gliding-SLICE-method (Schumann et al., 2009) for a combined investigation of intratidal compliance and resistance.

We hypothesised that both intratidal $R(V)$- and $C(V)$-profiles can be simultaneously analysed and that intratidal $R(V)$-profiles change depending on PEEP, V_T and possibly the underlying mechanical lung properties. Simultaneous monitoring of intratidal $C(V)$- and $R(V)$-profiles could help to assess lung status at bedside.

2. Methods

2.1. Animal data

Two different study groups were investigated under a variety of PEEP/V_T-settings. Nine lung-healthy piglets (23–29 kg) were premedicated with tiletamine 2.2 mg kg^{-1} + zolazepam 6 mg kg^{-1} (Zoletil, Virbac, Carros, France). After IV induction with ketamine 8 mg kg^{-1} and morphine 1 mg kg^{-1}, an aesthesia was maintained with IV infusion of ketamine 20 mg kg^{-1} h^{-1} and morphine 0.5 mg kg^{-1} h^{-1}. Animals were paralysed with Pancuronium. A 10 mL kg^{-1} IV bolus of dextran 60 was given to ensure relative normovolemia at all PEEP levels and 10 mL kg^{-1} h^{-1} Ringer acetate was administered IV. Animals remained in supine position throughout the experiment. Their trachea was intubated with a 9.0 mm endotracheal tube (Mallinckrodt, Athlone, Ireland) and their lungs were ventilated with a Servo^i ventilator (Maquet, Solna, Sweden). V_T was 4.6 mL/kg bodyweight (BW) and the inspired fraction of oxygen (FiO_2) 1.0. Respiratory rate and V_T were obtained from a pneumotachograph (Series 3700, Hans Rudolph Inc., Shawnee, KS), pressure measurements by a transducer (TSD104a, BIOPAC System Inc., Goleta, CA, USA). Respiratory data were acquired at 1000 Hz with a BICORE monitoring system (MP150, BIOPAC System Inc., Goleta, CA, USA) and resampled to 250 Hz. Before starting the ventilation protocol, a recruitment maneuver (volume-controlled ventilation for 2 min with PEEP = 10 cmH_2O and increasing V_T until p_{peak} = 40 cmH_2O) was carried out. Without changing V_T, PEEP was set to 0, 4, 6, 8, 16 cmH_2O in randomised order remaining in volume-controlled (constant flow) mode.

Please note that healthy animals were part of an experiment for comparison of mechanical ventilation to spontaneous breathing (Vimláti, unpublished results).

In 15 piglets (25–32 kg) under the identical anaesthetic regime, lung injury was induced by broncho-alveolar lavage 10 times with 50–60 mL/kg BW of saline solution (Lichtwarck-Aschoff et al., 1992; Nielsen et al., 1991). Ventilation was performed as described above except with a Servo-300 ventilator (Siemens-Elema, Solna, Sweden) and recorded at 100 Hz. Prelavage conditions were V_T = 12 mL/kg BW at PEEP = 0 cmH_2O. After stabilisation, animals were ventilated at PEEP-levels of 0 and 12 cmH_2O and V_T of 8, 12 and 16 mL/kg BW set in randomised order remaining in volume-controlled (constant flow) mode. Inspiration times were held constant.

All experiments were approved by the local Ethics Committee and the study was conducted in conformity with the National Institutes of Health guidelines in the laboratories of the Department of Surgical Sciences, University of Uppsala.

2.2. Data analysis

We carried out low-pass filtering on the expiratory data to eliminate disturbances from cardiogenic oscillations in the breathing signal (Lozano-Zahonero et al., 2014). Tracheal pressures were estimated from airway pressures taking the mechanical properties of the endotracheal tube into account (Guttmann et al., 1993). R and C during inspiration and expiration were assessed from the respiratory data using the gliding-SLICE method (Schumann et al., 2009): the inner 10–90% volume range of the tidal PV-loop was divided into 21 overlapping volume slices. For each slice the equation of motion of the respiratory system $p = p_0 + \frac{1}{C} \times V + R \times \dot{V}$ was solved for R, C and the dynamic pressure base p_0. $C(V)$-profiles were classified into purely increasing (I) i.e. increasing/horizontal (IH), purely horizontal (H), decreasing/horizontal (DH) i.e. purely decreasing (D), or increasing/horizontal/decreasing (IHD) as described in (Buehler et al., 2014).

2.3. Classification of the resistance–volume profiles

Eyeballing to decide whether a particular $R(V)$-profile runs a horizontal or a concave course is prone to error. For each animal