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Regional distribution of lung compliance by image analysis of computed tomograms☆

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ABSTRACT

Computed tomography (CT) can yield quantitative information about volume distribution in the lung. By combining information provided by CT and respiratory mechanics, this study aims at quantifying regional lung compliance (CL) and its distribution and homogeneity in mechanically ventilated pigs. The animals underwent inspiratory hold maneuvers at 12 lung volumes with simultaneous CT exposure at two end-expiratory pressure levels and before and after acute lung injury (ALI) by oleic acid administration. CL and the sum of positive voxel compliances from CT were linearly correlated; negative compliance areas were found. A remarkably heterogeneous distribution of voxel compliance was found in the injured lungs. As the lung inflation increased, the homogeneity increased in healthy lungs but decreased in injured lungs. Image analysis brought novel findings regarding spatial homogeneity of compliance, which increases in ALI but not in healthy lungs by applying PEEP after a recruitment maneuver.

1. Introduction

Acute lung injury (ALI) comprises heterogeneously distributed morphological changes in the lung parenchyma causing ventilation inhomogeneity. During mechanical ventilation, the heterogeneous lung-elastic pattern can be part of ventilation-associated lung injury (VALI) by causing injurious strain between neighboring lung units (Mead et al., 1970; Steinberg et al., 2004). The elastic properties of the lung can be studied by plotting volume against pressure (V/P) as is commonly done to assess lung function impairment in lung disease (Rahn et al., 1946). In intensive care, the lung V/P curve can serve as a guide for titrating mechanical ventilation, by adjusting the inspiratory airway pressure and the positive end-expiratory pressure (PEEP) so that the ventilation pressure is located on the steep part of the V/P curve (Amato et al., 1998). The V/P curve is the mean of different curves from different lung compartments so any adjustment of a ventilator setting presumably will not fit all compartments. Awareness that a heterogeneous lung-elastic pattern can cause ventilator-induced lung injury (VILI) by causing strain between neighboring lung units is increasing (Mead et al., 1970; Steinberg et al., 2004). Efforts have also been made to visualize or compute the regional heterogeneity of lung mechanics (Wellman et al., 2012). A basic presentation of such heterogeneity should be the distribution of the elastic characteristics of the lung, a "compliance map." To make it possible, regional changes in lung volume for a given change in pressure must be measured. Computed tomography (CT) can yield information about gas volume distribution (Simon, 2005). Difficulties arise when the topographic location of mechanical properties must be inferred from images obtained at different gas volumes (Simon et al., 2005). Lung aeration and the shape of the lung (as well as the corresponding position of bronchi, vessels, etc.) change in all three dimensions as the lung is inflated. This requires new approaches for studying lung morphology and mechanics. Guerrero et al. (2006) and Kaczka et al. (2011) proposed a method

☆ The study was performed at the Hedenstierna Laboratory, University Hospital, Uppsala, Sweden.

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for drawing a compliance map of the ventilated lung. However in the Guerrero et al. paper, the pressure step between the images was large, and in the Kaczka et al. study, animals were ventilated using forced oscillation, which in both cases limited the applicability of the techniques. The aims of the present study were as follows:

- To assess the topographic distribution and the degree of homogeneity of lung compliance in healthy and acutely injured lungs, at different PEEP levels.
- To establish the relationship between regional compliance and global compliance by measuring the pressure and volume at the airway opening.
- To estimate the relation between regional compliance homogeneity and the corresponding V/P curve.

2. Methods

2.1. Animal model

Four initially healthy pigs (weight 26.7 ± 2.7 kg), were examined exclusively for the present study and were not part of any other study. The study was conducted in adherence with the European Union Directive 2010/63/EU for animal experiments and was approved by the local animal ethics committee at Uppsala University. The animals underwent general anesthesia: after induction by intramuscular injection of atropine (0.04 mg/kg), tiletamine-zolazepam (5 mg/kg, Zoletil; Boeringer Ingelheim, Copenhagen, Denmark), and medetomine (5 μg/kg, Dormitor vet; Orion Pharma, Sollentuna, Sweden), anesthesia was maintained by intravenous infusion of ketamine (20 mg/kg/h, Ketaminol; Vetpharma, Zurich, Switzerland), fentanyl (5 mg/kg/h, Pharmalink, Spånga, Sweden), and pancuronium (0.24 mg/kg/h, Pavulon; Organon Teknika, Gothenburg, Sweden) in buffered glucose 2.5% (Rehydrex; Fresenius Kabi, Uppsala, Sweden) delivered at a rate of 7 ml/kg/h. The trachea was intubated via surgical tracheostomy, by using a cuffed tube (6.0 HI-CONTOUR; Mallinckrodt Medical, Athlone, Ireland) just before muscle relaxants were administered.

An 18-gauge catheter was introduced into the right internal jugular vein, together with a floating tip pulmonary artery (PA) catheter (Swan-Ganz thermodilution SP5107H, 7F, 110 cm, Baxter, Irvine, CA, USA). The latter was correctly positioned with the guidance of the PA pressure recording on the connected bedside monitor (SC 9000 XL, Siemens Medical Systems Inc., Danvers, MA, USA), and was used to assess cardiac output. The latter was measured in triplicate, by cold saline injected randomly during the respiratory cycle. Blood temperature was continuously monitored by the thermistor located on the PA catheter. Systemic blood pressure was determined by using an 18-gauge catheter inserted into the left carotid artery. A transcutaneous sensor on the ear measured oxyhemoglobin saturation (SpO_2). A mainstream sensor on the artificial airway provided a continuous carbon dioxide (CO_2) concentration in the respiratory gases. A urinary catheter was surgically inserted in the bladder to monitor urinary output.

An esophageal catheter (Oesophageal Catheter, Erich Jaeger GmbH, Höchberg, Germany) was positioned in the distal third of the esophagus, according to the technique recommended by Baydur et al. (1982) and another balloon catheter in the stomach to continuously measure the esophageal (P_{ESO}) and gastric pressure (P_{GA}). Pressure and flow were continuously measured at the airway opening (P_{AW} and V'_{AW}, respectively).

P_{AW}, P_{ESO}, and P_{GA} were measured with three different pressure transducers (DigimaClic Pressure Transducers, Special Instruments GmbH, Nördlingen, Germany). V'_{AW} was acquired with a Fleisch pneumotacograph (Laminar Flow Element type PT, Special Instruments GmbH, Nördlingen, Germany) positioned between the endotracheal tube and the ventilator; a differential pressure transducer (Diff-Cap Pressure Transducer, Special Instruments GmbH, Nördlingen, Germany) sampled the signals from the pneumotacograph. All signals were forwarded to an analog-to-digital converter card (DAQ-card AI-16XE50, National Instruments Corp., Austin, TX, USA) and stored on a personal computer (Intel Centrino, Intel Corp., Santa Clara, CA, USA) at a sampling frequency of 200 Hz, using the BioBench Software (ver.1.0, National Instruments Corp., Austin, TX, USA). Insufflated and exhaled volumes (V_{AW}) were calculated according to the flow integration. Baseline ventilation was provided by a mobile ventilator (Servo-I, Maquet, Solna, Sweden) and consisted of a constant flow, volume-controlled mode with a tidal volume (V_T) of 9 ml/kg; an inspiratory-to-expiratory (I:E) ratio equal to 1:2, a respiratory rate (RR) of 20 breaths per minute, positive end-expiratory pressure (PEEP) of 5 cm H_2O, and fraction of inspired oxygen (FiO_2) set to 0.5. After instrumentation, the animals were allowed to stabilize for the following 60 min.

2.2. Protocol design

The protocol for the CT exposures at various ventilatory patterns and inspired volumes has been presented in a previous paper (Perchiazzi et al., 2011) and is only summarized here (see Fig. 1). The animals, after they had been positioned on the CT table (Somatom Sensation 16, Siemens, Erlangen, Germany), underwent a recruitment maneuver (RM) consisting of a constant airway pressure of 40 cmH_2O for 40 s (Lapinsky and Mehta, 2005). The inspiratory capacity (IC) was computed by measuring the inspired volume when a constant pressure of 40 cm H_2O was applied for 20 s. Then the pigs underwent 12 inspiratory hold maneuvers (IHMs) at different inspiratory volumes that covered the IC (V_T = (IC/12) × 1, (IC/12) × 2, (IC/12) × 3, up to IC) and were administered as monotonic increasing volumes. Two to three min of tidal breathing separated consecutive IHMs, in order to restore steady state ventilation. Spiral CT scans of the entire lung were executed simultaneously as each IHM (120 kV, 80 mA s) and at zero end expiratory pressure (ZEEP); they lasted about 5–6 s each. The sequence described (RM followed by exposures at 12 IHMs at two levels of PEEP, followed by ZEEP) was performed in each animal, before and after an ALI was induced. The four conditions were normal healthy lungs at PEEP 5 and 10 [cm H_2O] (labeled NL5 and NL10, respectively) and ALI lungs at PEEP 5 and 10 [cm H_2O] (labeled ALI5 and ALI10, respectively).

From the stack of images generated by the CT scanner during each IHM, we chose to analyze five transverse planes per IHM, covering the lung from the paradiaphragmatic to the apical level. The distance on the longitudinal axis from the paradiaphragmatic CT scan plane to the most apical one was fixed at 100 mm, the five transverse planes were equally spaced by 25 mm, and slice thickness was 5 mm. Images from parts of the lung other than the chosen planes were discarded. The images were selected and analyzed by using scripts for the Image Processing Toolbox and Statistics Toolbox for MatLab R2010 (MatLab, The MathWorks, Natick, MA, USA), purposely written by one of the authors (G.P.). Lung parenchyma was manually outlined in each slice, avoiding automatic segmentation algorithms, which might have introduced flaws in separating atelectatic areas from chestwall structures.

Moreover, since CT technology measures density, the image analysis and segmentation were internally validated by verifying the constancy of the tissue volume across the pressure steps (Simon, 2000).

2.3. Lung injury

Lung injury was induced by injecting oleic acid (OA) 0.1 ml/kg (Apoteksbolaget, Göteborg, Sweden) into the central venous