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# Esophageal pressure as an estimate of average pleural pressure with lung or chest distortion in rats

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ABSTRACT

Pressure–volume curves of the lungs and chest wall require knowledge of an effective 'average' pleural pressure ($Ppl_{av}$), and are usually estimated using esophageal pressure as $P_{L_{es}}$–V and $Pw_{es}$–V curves. Such estimates could be misleading when *P*pl becomes spatially non-uniform with lung lavage or shape distortion of the chest. We therefore measured $P_{L_{es}}$–V and $Pw_{es}$–V curves in conditions causing spatial non-uniformity of Ppl in rats. $P_{L_{es}}$–V curves of normal lungs were unchanged by chest removal. Lung lavage depressed $P_{L_{es}}$–V but not $Pw_{es}$–V curves to lower volumes, and chest removal after lavage increased volumes at $P_L \geq 15\ cmH_2O$ by relieving distortion of the mechanically heterogeneous lungs. Chest wall distortion by ribcage compression or abdominal distension depressed $Pw_{es}$–V curves and $P_{L_{es}}$–V curves of normal lungs only at $P_L \geq 3\ cmH_2O$. In conclusion, Pes reflects $Ppl_{av}$ with normal and mechanically heterogeneous lungs. With chest wall distortion and dependent deformation of the normal lung, changes of $P_{L_{es}}$–V curves are qualitatively consistent with greater work of inflation.



## 1. Introduction

Pleural surface pressure (*P*pl) is a clinically relevant parameter, the information it provides being useful in patient management during weaning (Jubran et al., 2005) and in the choice of positive end expiratory pressure (PEEP) in acute respiratory distress syndrome (ARDS) patients (Talmor et al., 2008). As direct measurements are impractical, esophageal pressure (Pes), usually obtained with the esophageal balloon technique, is commonly used to estimate Ppl in humans. Estimation of *P*pl from Pes allows assessment of in situ transpulmonary ($P_{L_{es}}$) and transthoracic pressure ($Pw_{es}$) for determining lung and chest wall mechanics and respiratory muscle action.

There are practical concerns about the use of Pes in patients (de Chazal and Hubmayr, 2003) because of a variety of possible artifacts (Milic-Emili, 1984; Washko et al., 2006). Of greater concern is the fact that Ppl is not spatially uniform, as demonstrated by direct measurements in several animal species (Hoppin et al., 1969; D'Angelo et al., 1970; Agostoni and D'Angelo, 1971) and, indirectly, in humans (Milic-Emili et al., 1966). As a consequence, Ppl estimated by means of the esophageal balloon technique is customarily regarded as an effective 'average' pleural pressure, ($Ppl_{av}$), which is here defined as the spatially uniform pleural surface pressure that would be required to attain the observed lung volume and flow.

The use of Pes as an estimator of $Ppl_{av}$ has become a well accepted procedure in the presence of a normal respiratory system, and is justified by experiments in normal supine animals that show (a) the transpulmonary pressure–volume curves measured using Pes ($P_{L_{es}}$–V) are similar to those measured in the excised lung (Wohl et al., 1968; Lai and Hildebrandt, 1978), and (b) the average value of local elastic recoil pressures measured directly through pleural windows at functional residual capacity is similar to the transpulmonary pressure measured at the same volume after wide opening of the chest, irrespective of body position (D'Angelo et al., 1970). In humans, this conclusion has been indirectly supported by the observation that the shape of the $P_{L_{es}}$–V curve is similar in different postures (Milic-Emili, 1984). Taken together, these findings suggest that in the presence of a normal respiratory system, Pes reflects $Ppl_{av}$.

In contrast, the use of Pes in pathological conditions has been questioned, because the degree of spatial non-uniformity of Ppl can increase markedly, and the more Ppl is non-uniform, the less likely Pes is to represent $Ppl_{av}$ (de Chazal and Hubmayr, 2003). Such non-uniformity could result from marked chest deformities or abdominal distension (Talmor et al., 2006; Behazin et al., 2010), or because of heterogeneous lung mechanical properties, as in ARDS (Maunder et al., 1986), moderate-to-severe COPD, cystic fibrosis, or pulmonary edema. If distortion is not marked, as is usual under physiological conditions, the ability of Pes to represent $Ppl_{av}$ can be evaluated by the degree of similarity of the

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transpulmonary pressure–volume curves obtained before and after wide opening of the chest, as mentioned above. In the presence of marked lung isovolume distortion by the chest, this criterion may no longer be satisfied, because shape distortion by itself changes the lung's mechanical characteristics, making it less compliant. Thus, the transpulmonary pressure–volume curves obtained before and after opening of the chest would be expected to differ according to the degree to which the lung is distorted from its unconstrained shape.

In this study, we tested the ability of Pes to estimate $Ppl_{av}$ under conditions expected to cause marked spatial non-uniformity of lung mechanical properties or marked distortion due to an increased mismatch between intrinsic lung and chest wall shapes. Heterogeneity of regional mechanical properties reproducing an ARDS-like condition was obtained by repeated lung lavage. Lavage-induced heterogeneity should principally affect the lung and only marginally the chest wall, because the lung is more easily deformed, and lung-chest wall uncoupling with massive pneumothorax does not modify the relationship between transthoracic pressure and rib cage diameters in supine animals (D'Angelo et al., 1973). Moreover, no changes in the mechanical properties of the chest wall should occur with lung lavage. As a consequence, the volume–pressure curves of the relaxed chest wall obtained before and after surfactant depletion should be similar. This would support the use of Pes to estimate $Ppl_{av}$ even in the presence of marked spatial non-uniformity of lung mechanical properties and parenchymal distortion.

In addition, we have investigated the changes of the $P_{Les}$–V curve that occur with abdominal distension or rib cage compression causing marked shape distortion. Finally, to confirm our ability to reproduce results found in previous studies, we checked whether in normal rats the lung P–V curves recorded before and after widely opening the chest are superimposable.

## 2. Methods

Sixteen male Sprague-Dawley rats (weight range 390–480 g) were premedicated with diazepam (10 mg $kg^{-1}$) and anesthetized with an intraperitoneal injection of pentobarbital sodium (40 mg $kg^{-1}$) and chloral hydrate (170 mg $kg^{-1}$). The animals were kept supine throughout the experiment. The trachea was cannulated, and polyethylene catheters were inserted into the jugular vein and carotid artery. A balloon-tipped catheter (inner diameter 0.6 mm) was placed in the lower third of the esophagus. The balloon was 20 mm long and 3 mm wide. In those animals in which abdominal distension was produced by inflating a 5 cm long rubber balloon advanced under the linea alba, a balloon similar to the esophageal one was placed between the diaphragm and the liver.

Airflow was measured with a heated Fleisch pneumotachograph no. 0000 (HS Electronics, March-Hugstetten, Germany) and differential pressure transducer (Validyne MP45, ±2 $cmH_2O$; Northridge, CA). The response of the pneumotachograph was linear over the experimental flow range. Pressures in the trachea (Ptr), esophagus, abdomen and systemic blood pressure were measured with pressure transducers (8507C-2 Endevco, San Juan Capistrano, CA; Statham P23Gb, Gould Electronics, Valley View, OH) connected to the side arm of the tracheal cannula, the esophageal and abdominal balloons, and carotid catheter, respectively. The appropriate positioning of the esophageal balloon was tested by measuring the ratio $\Delta Pes/\Delta Ptr$ during rapid, manual rib cage compressions with closed airways, similar to the occlusion test performed during spontaneous breathing (Baydur et al., 1982). There was no appreciable lag in the *P*es signal or alteration in amplitude up to 20 Hz. The signals from the transducers were amplified (RS3800; Gould Electronics, Valley View, OH), sampled at 200 Hz by a 12-bit A/D converter (AT MIO 16E-10; National Instruments, Austin, TX), and stored on a desktop computer. Volume changes ($\Delta V$) were obtained by numerical integration of the digitized airflow signal.

After completion of the surgical procedure, the rats were paralyzed with pancuronium bromide (1 mg $kg^{-1}$) and ventilated with a specially designed, computer-controlled ventilator (D'Angelo et al., 2008), delivering water-saturated air from a high pressure source (4 atm) at constant flow, while Ringer-bicarbonate was continuously infused intravenously at a rate of 4 ml $kg^{-1}$ $h^{-1}$, and epinephrine occasionally administered to maintain normal arterial blood pressure. Anesthesia and complete muscle relaxation were maintained with additional doses. Adequacy of anesthesia was judged from the absence of any sudden increase in heart rate and/or systemic blood pressure.

The pressure across the respiratory system, the transthoracic and in situ transpulmonary pressures were obtained as Prs = Ptr, $Pw_{es}$ = Pes, and $P_{Les}$ = Ptr–Pes, respectively, whereas $P_L$ was used to indicate transpulmonary pressure in the presence of a spatially uniform Ppl, as it is the case with widely open chest, except for the small contact area in the lowermost part of the lung. Because measurements were performed in paralyzed animals under nearly static conditions (see below), these pressures essentially reflect the elastic properties of lung and chest wall.

### 2.1. Procedure and data analysis

Mechanical ventilation parameters included a tidal volume ($V_T$) of 8 ml $kg^{-1}$, inspiratory time 0.25 s, expiratory time 0.5 s, and an end-inspiratory pause of 0.2 s. These ventilator settings were maintained throughout the experiment. Flow was continuously integrated and displayed to monitor lung volume changes.

Three inflation P–V curves were obtained before (control) and during any given intervention by slowly inflating (~1 ml $s^{-1}$) the respiratory system from Ptr = 0 to Ptr = 30 $cmH_2O$. Before each series of measurements the lungs were inflated 3–4 times to a Ptr of ~26 $cmH_2O$ to ensure a uniform volume history. After each P–V curve, the lungs were allowed to deflate, and the expiratory valve was connected to a drum in which pressure was set to –20 $cmH_2O$, the expired volume being the difference between the end-expiratory and minimal gas (or residual) volume (EELV-RV). Vital capacity (VC) was defined as sum of the inflation volume between Ptr 0 and 30 $cmH_2O$ and EELV-RV. Finally, the compliance of the respiratory system (Crs), chest wall (Cw), and lung ($C_L$) were computed as the slope of each P–V curve in the volume range of the linear part of the control P–V curve.

In 9 rats, respiratory mechanics were assessed after the induction of acute lung injury by repeated intratracheal instillations and withdrawals of warm (38 °C) physiological saline, in aliquots of 30 ml $kg^{-1}$, until arterial oxygen tension fell below 80 mmHg. During the intervals between lavages and after lavage, the animals were ventilated with oxygen (90%) and a positive end-expiratory pressure (PEEP) of 6 $cmH_2O$.

In 7 rats, respiratory mechanics was assessed during rib cage compression with a rubber sheet and a Velcro band, which also provided moderate and marked restriction, respectively, or during abdominal distension obtained by inflating the abdominal balloon to increase subdiaphragmatic pressure to ~7 $cmH_2O$ (moderate distension) and to ~21 $cmH_2O$ (marked distension). Thereafter compression and distension were removed and respiratory mechanics reassessed.

The animals were killed with an overdose of anesthetic, and respiratory mechanics were measured again. The ventilator was disconnected, the silicon tube between the tracheal cannula and the pneumotachograph was clamped, and the thorax was quickly and widely opened, Ptr being continuously monitored. The increase of Ptr upon opening the chest ($\Delta Ptr,oc$) was taken to represent $-Ppl_{av}$