Effects of unilateral hyperinflation on the interpulmonary distribution of pleural pressure

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HUBMAYR, ROLF D., AND SUSAN S. MARGULIES. Effects of unilateral hyperinflation on the interpulmonary distribution of pleural pressure. J. Appl. Physiol. 73(4): 1650-1654, 1992.—Motivated by single lung transplantation, we studied the mechanics of the chest wall during single lung inflations in recumbent dogs and baboons and determined how pleural pressure (Ppl) is coupled between the hemithoraces. In one set of experiments, the distribution of Ppl was inferred from known volumes and elastic properties of each lung. In a second set of experiments, costal pleural liquid pressure (Pplcos) was measured with rib capsules. Both methods revealed that the increase in Ppl over the ipsilateral or inflated lung (∆Ppl) is greater than that over the contralateral or noninflated lung (∆Ppl). Mean d(∆Ppl)/d(∆Ppl) and its 95% confidence interval was 0.7 ± 0.1 in dogs and 0.5 ± 0.1 in baboons. In a third set of experiments in three dogs and three baboons, we evaluated whether anatomic pathways such as the rib cage and diaphragm-abdomen contribute to pressure coupling between the hemithoraces.

METHODS

Eleven dogs (20-35 kg) and three baboons (12-15 kg) were anesthetized with pentobarbital sodium (25-30 mg/kg) and studied in the supine posture. Dogs were intubated translaryngeally with a Y-shaped dual-lumen endotracheal tube (Kottmeyer, Rusch). In baboons, the left main stem bronchus was intubated with a Robertshaw dual-lumen endotracheal tube through a tracheostomy. The position of the endotracheal tube was adjusted under endoscopic guidance to ensure patency of all lobar bronchi. The animals were mechanically ventilated with a Harvard pump. A balloon catheter was placed in the mid- to lower third of the esophagus for the measurement of intrathoracic pressure (Pes). The position of the esophageal balloon catheter was adjusted until the change in Pes during inspiratory efforts against an occluded airway fell to within 1 cmH₂O of the change in airway pressure (Pao) (2). Right and left Pao were recorded from the proximal ends of the respective endotracheal tube lumina. Gas flow (V) to each lung was measured with separate pneumotachographs (Fleisch no. 2) and differential pressure transducers (Validyne MP 45). Pressure and V signals were displayed on a strip chart recorder (Hewlett-Packard) and stored on a computer (DEC 11/70). The change in right and left lung volumes was determined by computer integration of the digitized flow signals. The relaxation volume (Vrel) of each lung were measured with an N₂ equilibration technique (5). The resident gas of the lung(s) at Vrel was equilibrated with a known volume of O₂. This was accomplished by five slow manual inflations and deflations of the lung(s) with a calibrated supersyringe. The N₂ concentration before and after equilibration was measured with a mass

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MOTIVATED by the introduction of single lung transplantation into clinical practice, our aim is to define the mechanisms that govern the interactions between two lungs with different mechanical properties. In trying to understand how lung-lung interactions affect the interpulmonary distribution of ventilation, we propose the hypothesis that under some circumstances the two lungs are exposed to different mean surface or pleural pressures (Ppl). One such condition may exist when a dynamically hyperinflated emphysematous lung operates in parallel with a smaller implant. To test this hypothesis, we evaluated the interpulmonary distribution of Ppl during single lung inflations in normal recumbent dogs and baboons. Dogs were studied in anticipation of further experiments with a canine model of unilateral emphysema (14, 17, 19). In addition, we made measurements in baboons because of their greater anatomic similarity to humans.

In this paper, we present the results of three sets of experiments to test the hypothesis that there are side-to-side differences in mean Ppl when lungs and chest wall are deformed by single lung inflation. In the first set of experiments on seven dogs and three baboons, the interpulmonary distribution of Ppl was inferred from known volumes and elastic properties of each lung (indirect method). In the second set of experiments in four additional dogs, we made direct measurements of costal pleural liquid pressure (Pplcos) during single lung inflations (20). In the third set of experiments on three dogs and three baboons, we evaluated whether anatomic pathways such as the rib cage and diaphragm-abdomen contribute to pressure coupling between the hemithoraces.
spectrometer (Centronic, Croyton). By use of this technique, Vrel values fell within 5% of those measured with plethysmography (15).

Rib capsule technique. In four dogs, Ppl_{cap} was measured directly from rib capsules (20). Overlying tissue was removed from the third, fourth, and/or fifth ribs along both midaxillary lines. Small holes (2 mm diam) were drilled through the ribs, leaving the parietal pleura intact. A plastic intravenous tubing adapter was placed into the hole and glued to the rib. Polyethylene tubing was connected to the adapter, filled with methylene blue-colored saline, and capped with a rubber stopcock. The capsule was then anchored to the rib with screws and dental acrylic. An 18-gauge needle attached to a fluid-filled catheter was introduced through the rubber stopcock, and the parietal pleura was perforated. Then the polyethylene catheter was clamped to avoid air entry into the pleural space, the needle and rubber stopcock were removed, and the capsule was connected to a liquid-filled pressure transducer assembly (Cobe Lab, Lakewood, CO). Pressure recordings were taken only from rib capsules that met the following frequency-response criteria and gave reproducible readings. Ppl_{cap} tracings had to show cardiogenic oscillations and reach a new pressure plateau 10 s after a step change in lung volume. A lateral chest X-ray was taken during each experiment to guard against inclusion of data from dogs with a pneumothorax. In supine dogs, a pneumothorax causes the heart to drop away from the sternum toward the spine. The lungs were also inspected postmortem under water for needle puncture marks and air leaks.

Experimental protocol. After muscle paralysis was induced with pancuronium bromide (0.2 mg/kg), both lungs were inflated to total lung capacity (TLC) to provide a constant volume history. TLC of each lung was defined as the volume at a Pao of 30 cmH₂O. Subsequently, the respiratory system was inflated from Vrel in small volume steps, exposing both lungs to the same alveolar pressure. This was done with a calibrated syringe attached to a Y port that connected the two lumina of the endotracheal tube. From the recorded pressures and integrated flows, separate inflation pressure-volume curves were constructed for each lung. Only for maneuvers during which both lungs were inflated simultaneously to a common airway pressure was transpulmonary pressure (Ptl) defined as the difference between Pao and Pes.

After an inflation of both lungs to TLC, one lung was inflated from Vrel in small volume steps while the lumen of the endotracheal tube leading to the contralateral lung was occluded. Complete separation between ipsilateral (side of inflation) and contralateral airways was assumed if a constant pressure difference could be maintained at each inflation step. Right and left single lung inflations were repeated in random order.

Unilateral inflation measurements were repeated in three of the seven dogs and in all baboons after minimization of possible contributions of rib cage and diaphragm-abdomen pathways to pressure transmission between the hemithoraces. First, two hooks were screwed into the sternum and rigidly attached to a stationary steel bar, preventing any sternal motion during single lung inflation. Second, the abdomen was opened through a midline incision, and the abdominal contents were moved to expose a large portion of the abdominal surface of the diaphragm to atmospheric pressure.

Rationale for data handling (indirect method). It was necessary to make two assumptions to derive the Ppl distribution during single lung inflation from Pes, Pao, and lung volume measurements. Their validity is considered in the discussion. The first assumption is that Ppl increases uniformly during bilateral lung inflations and that, under these conditions, the change in Pes (ΔPes) reflects the increase in average Ppl within both hemithoraces (3, 21). On the basis of this assumption, we constructed right and left lung Ptl-volume curves from the Pao, Pes, and bronchoscopic volume measurements during bilateral lung inflation and computed their respective inflation compliances (CL). The second assumption is that, at volumes near Vrel, the lungs are fluidlike and their elastic properties can be described by a single compliance (6). Consequently, each lung's Ptl-volume curve can be used to predict its corresponding Ptl during bilateral and single lung inflations.

Specifically, the change in ipsilateral Ppl (ΔPpl_i) during single lung inflation from Vrel was computed from the difference between the change in measured ipsilateral airway pressure (ΔPao_i) and an estimated change in ipsilateral transpulmonary pressure (ΔPli)

\[ ΔPli = ΔPao_i - ΔPao_c \]  

(1)

ΔPli was estimated from the known ipsilateral CL (CL_i) and from the ipsilateral volume increase (ΔV_i) above Vrel

\[ ΔPli = ΔV_i/CL_i \]  

(2)

Substitution of Eq. 2 into Eq. 1 results in the relationship used to estimate ΔPpl during unilateral lung inflation

\[ ΔPpl_i = ΔPao_i - ΔV_i/CL_i \]  

(3)

Similarly, the change in contralateral Ppl (ΔPpl_c) is given by the relationship

\[ ΔPpl_c = ΔPao_c - ΔV_c/CL_c \]  

(4)

However, the volume of the contralateral lung (V_c) was held constant at Vrel (ΔV_c = 0). Therefore

\[ ΔPpl_c = ΔPao_c \]  

(5)

Statistical methods. The relative rates of change in Ppl and Ptl during single lung inflations were computed using a linear regression analysis. Regression slopes [d(ΔPpl_i)/d(ΔPpl_c)] and their 95% confidence intervals were derived for both indirect and direct Ppl measurements in dogs and baboons. The effects of experimental interventions, such as sternal fixation, on the regression slopes were compared using a one-factor analysis of variance for repeated measures.

RESULTS

Figure 1 shows a comparison of the indirect ΔPpl_i and ΔPpl_c estimates from seven dogs. The slope of the regression line of 0.7 ± 0.1 (significantly different from 1, P ⩽ 0.05) underscores that in the recumbent dog the average rise in Ppl during single lung inflation is nonuni-
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Figure 1. Comparison of change in estimated pleural pressure (indirect method) over ipsilateral ($\Delta P_{pl_i}$, abscissa) and contralateral ($\Delta P_{pl_c}$, ordinate) lung during single lung inflation in 7 dogs (each represented by different symbol). Each data point represents mean of 3 measurements during right or left lung inflation. Solid line, line of identity. Broken line was computed by linear regression analysis. Slope of regression line is $0.7 \pm 0.1$ (significantly different from 1, $P < 0.05$).

Figure 2 shows a comparison of the changes in ipsilateral and contralateral pleural liquid pressures ($\Delta P_{pl_i}$, abscissa) and contralateral ($\Delta P_{pl_c}$, ordinate) lung during single lung inflations in recumbent dogs. Data are from 5 rib capsules in 4 animals. Each data point represents mean of 3 inflations. Solid line, line of identity. Slope of regression line is $0.7 \pm 0.1$ (significantly different from 1, $P < 0.05$).

Figure 3 shows a comparison of change in costal pleural pressure (direct method) over ipsilateral ($\Delta P_{pl_i}$, abscissa) and contralateral ($\Delta P_{pl_c}$, ordinate) lung during single lung inflations in recumbent dogs. Data are from 5 rib capsules in 4 animals. Each data point represents mean of 3 inflations. Solid line, line of identity. Slope of regression line is $0.7 \pm 0.1$ (significantly different from 1, $P < 0.05$).

Figure 4 shows $\Delta P_{pl_i}$, $\Delta P_{pl_c}$, and the corresponding regression slopes of 3 dogs and 3 baboons measured under four experimental conditions. Sternal fixation and exposure of the abdominal diaphragm surface to atmospheric pressure had no significant impact on the regression slopes in either dogs or baboons. For dogs the slopes of the regression lines were $0.6, 0.5, 0.5, \text{ and } 0.5$, respectively ($\text{NS, } P > 0.05$). For baboons the slopes of the regression lines were $0.5, 0.5, 0.4, \text{ and } 0.4$, respectively ($\text{NS, } P > 0.05$).

DISCUSSION

Our data show that the mediastinal structures of both dogs and primates can support a pressure gradient when the lungs assume volumes and transpulmonary pressures that differ from each other. The pressure gradient reflects the resistance of the lungs and their boundary structures to displacement and deformation. Although single lung inflation produced a greater inhomogeneity in Ppl in baboons than in dogs, the small number of animals studied precludes a statistical comparison between species.

Estimation of hemithoracic Ppl: validity of assumptions. To compute estimates of $\Delta P_{pl_i}$ and $\Delta P_{pl_c}$ during single

Figure 3. Comparison of change in estimated pleural pressure (indirect method) over ipsilateral (abscissa) and contralateral (ordinate) lung during single lung inflation in 3 baboons. Each data point represents mean of 3 inflations. Data points were obtained as in Fig. 1. Solid line, line of identity. Slope of regression line is $0.5 \pm 0.1$ (significantly different from 1, $P < 0.05$). The capsule was inflated when the lung opposite the capsule was inflated. The slope of the linear regression through the measurements was $0.7 \pm 0.1$ (significantly different from 1, $P < 0.05$), which is identical to the slope of the regression derived from indirect Ppl estimates (Fig. 1).

Figure 3 shows the indirect $\Delta P_{pl_i}$ and $\Delta P_{pl_c}$ estimates during single lung inflations in three baboons. The slope of the linear regression is $0.5 \pm 0.1$, less than that in the recumbent dog. These results indicate a greater nonuniformity in the Ppl distribution during unilateral hyperinflation in baboons than in dogs.

Figure 4 shows $\Delta P_{pl_i}$, $\Delta P_{pl_c}$, and the corresponding regression slopes of three dogs and three baboons measured under four experimental conditions. Sternal fixation and exposure of the abdominal diaphragm surface to atmospheric pressure had no significant impact on the regression slopes in either dogs or baboons. For dogs the slopes of the regression lines were $0.6, 0.5, 0.5, \text{ and } 0.5$, respectively ($\text{NS, } P > 0.05$). For baboons the slopes of the regression lines were $0.5, 0.5, 0.4, \text{ and } 0.4$, respectively ($\text{NS, } P > 0.05$).
Based on measurements of dogs, there is good agreement, however, between APes-based measurements of compliance and regional volume is still unresolved. More specifically, it is unclear whether changes in shape alter the relationship between local Ppl and regional volume.

Despite intensive investigation, the extent to which mean Ppl over the two lungs can differ in dogs, given that the canine mediastinum contains only a thin transparent sheet of connective tissue that does not completely separate right from left hemithorax. However, the mediastinum is not a uniform structure and should not be compared with an elastic membrane. There are local barriers to displacement, such as the heart, the great vessels, and the trachea (which, in our experiment, was reinforced with an endotracheal tube). If the ipsilateral lung was sufficiently deformable (i.e., liquid), it would move easily around structures that resist displacement, whereby the mediastinal membrane itself may simply unfold without becoming stress bearing. In this scenario, there would be complete transmission of pressure between the hemithoraces. Because the ipsilateral lung becomes stiffer as its volume increases, it may not “flow” around local barriers. This may result in stress concentrations at the interfaces between the lung and thoracic midline structures and lead to incomplete pressure transmission to the contralateral hemithorax. The presence of defects within the mediastinal connective tissue is not important, because even near Vrel the lungs could not deform enough to flow through small openings.

The mediastinum is not the only lung boundary structure that is displaced during unilateral lung inflation. Inflation of the ipsilateral lung and hemithorax increases contralateral rib cage dimensions because of the connections between right and left ribs via the sternum and because an increase in abdominal pressure is transmitted through the apposing diaphragm to the lower contralateral hemithorax. By themselves, these mechanisms would lower the surface pressure over the contralateral lung. Because contralateral airway occlusion pressure and, thus, Ppl, invariably increased during ipsilateral lung inflation, these mechanisms must have been offset by pressure transmission through mediastinal pathways and by the action of abdominal pressure on the diaphragm-apposed lung surface. We were unable to demonstrate systematic differences in Ppl coupling after sternal fixation or after exposing the abdominal diaphragm to atmospheric pressure. The number of dogs and baboons in which we studied the effect of these interventions on Ppl transmission was small, and the results were variable and inconsistent across animals. Nevertheless, this negative finding supports the theory that the mediastinum is the prominent pathway for lung-lung interdependence.

One might be tempted to quantify lung-lung interdependence with a single mediastinal coupling compliance \( \Delta V / (\Delta P_{l} - \Delta P_{r}) \). Such a measurement would be useful,
however, only if it was independent of lung shape and stiffness, if it reflected only the displacement impedance of thoracic midline structures themselves, and if it was insensitive to the stress placed on the mediastinum before its displacement. For example, tissue attachments between diaphragm and thoracic midline structures may exert axial tension on the mediastinum. This would make the "so-called" mediastinal compliance sensitive to changes in diaphragm activity and chest wall shape and limit its predictive value as a simple determinant of the interpulmonary Ppl distribution. Although our study does not offer insights into the relative importance of these mechanisms, it does underscore that lungs with unequal size and elastic properties need not be exposed to the same surface pressure.

**Implication of results to lung mechanics in disease.** According to the classic model of Milic Emili et al. (11), the lung is an isotropic homogeneous elastic solid that is exposed to a vertical gradient in surface pressure when the chest wall is intact. At Vrel, dependent lung units are exposed to a greater surface pressure and assume a smaller volume than nondependent units. Given the nonlinear relationship between volume and Pt, the lung parenchyma of dependent units is less resistant to volume expansion and deformation. Thus, when all lung regions are exposed to the same change in Ppl, the topographical distribution of ventilation reflects primarily regional differences in lung elastic properties.

Stevens et al. (16) measured regional volumes and ventilation in two emphysematous patients who died shortly after single lung transplantation. They noted that the native emphysematous lung received a greater fraction of the inspired gas than the implant and concluded that this observation was produced by a parallel inhomogeneity in lung elastic properties. In an accompanying editorial, Bates (1) assumed that, during breathing, intraintrathoracic pressure changes uniformly over both lungs, reducing the determinants of the interpulmonary distribution of gas flow to lung resistance and compliance (12). Because blood flow to the implant exceeded that of the native emphysematous lung, single lung transplantation for patients with chronic obstructive pulmonary disease (COPD) was abandoned on the basis of the belief that the procedure would invariably cause interpulmonary ventilation-perfusion mismatch.

The recent success of single lung transplantation in patients with COPD raises questions about Stevens' observations and conclusions (9, 18). The findings in this communication challenge the assumption that lung surface pressure changes uniformly when the lungs operate at different volumes and transpulmonary pressures. Such a condition may exist if an emphysematous lung with expiratory flow limitation hyperinflates and starts to "compress" the contralateral implant. The extent to which implant volume and ventilation are affected by dynamic hyperinflation depends on the degree of pneumatic coupling between the hemithoraces.

**REFERENCES**


