Asymmetrical action of the canine diaphragm after single-lung inflation

André De Troyer,1,2 Dimitri Leduc,1,2 Pierre Alain Gevenois,3 and Matteo Cappello1,2

1Laboratory of Cardiorespiratory Physiology, Brussels School of Medicine, Brussels; and 2Chest Service and 3Department of Radiology, Erasme University Hospital, Brussels, Belgium

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De Troyer A, Leduc D, Gevenois PA, Cappello M. Asymmetrical action of the canine diaphragm after single-lung inflation. J Appl Physiol 110: 1519–1525, 2011. First published February 24, 2011; doi:10.1152/japplphysiol.01313.2010.—Single-lung transplantation (SLT) in patients with emphysema leads to a cranial displacement of the diaphragm on the transplanted side and a shift of the mediastinum toward the transplanted lung. The objective of the present study was to assess the effect of unilateral lung inflation on the mechanics of the diaphragm. Two endotracheal tubes were inserted in the two main stem bronchi of six anesthetized dogs, and radiopaque markers were attached along muscle fibers in the midcostal region of the two halves of the diaphragm. The animals were then placed in a computed tomographic scanner, the left or the right lung was passively inflated, and the phrenic nerves were stimulated while the two endobronchial tubes were occluded. As lung volume increased, the fall in airway opening pressure (ΔPao) in the inflated lung during stimulation decreased markedly, whereas ΔPao in the noninflated lung decreased only moderately (P < 0.001). Also, the two hemidiaphragms shortened both during relaxation and during phrenic stimulation, but the ipsilateral hemidiaphragm was consistently shorter than the contralateral hemidiaphragm. In addition, the radius of curvature of the ipsilateral hemidiaphragm during stimulation increased, whereas the radius of the contralateral hemidiaphragm remained unchanged. These observations indicate that 1) in the presence of unilateral lung inflation, the respiratory action of the diaphragm is asymmetric; and 2) this asymmetry is primarily determined by the differential effect of inflation on the length and curvature of the two halves of the muscle. These observations also imply that in patients with emphysema, SLT improves the action of the diaphragm on the transplanted side.

mechanics of breathing; respiratory muscles; single-lung transplantation; mediastinum

The diaphragm is sufficiently thin so that it can be regarded as a curved membrane. The pressure generated by the diaphragm in response to a given activation, therefore, is determined by the length of the muscle during contraction and by the radius of muscle curvature (10, 28). These two factors explain the effect of lung inflation on the change in pleural (ΔPpl) or airway opening pressure (ΔPao) that occurs when the airways in anesthetized dogs (19, 21, 22), cats (11, 21, 23), and rabbits (25) are occluded and the diaphragm is selectively activated by stimulation of the phrenic nerves. Thus, as the lungs in the animals are passively inflated from functional residual capacity (FRC) to total lung capacity (TLC) before stimulation, ΔPao (or ΔPpl) decreases markedly because 1) the length of the relaxed diaphragm and the elastance of the rib cage decrease, so that the muscle during contraction is shorter and generates less force; and 2) the radius of diaphragm curvature during contraction increases, so that the pressure developed for a given muscle force decreases (Laplace’s law) (10, 28).

Single-lung transplantation (SLT) has become a well-established treatment option for patients with advanced emphysema over the last 20 years. This procedure leads to a complex physiological setting, in that it places in the pleural cavity an emphysematous (native) lung and a normal (transplanted) lung, i.e., two lungs with different sizes and different elastic properties. As a result, in patients with SLT for emphysema, the hemidiaphragm adjacent to the transplanted lung is more cranial than the hemidiaphragm adjacent to the native lung, and the mediastinum is shifted laterally toward the transplanted lung (3).

In an attempt to assess the implications of this arrangement on diaphragm function, Hubmayr et al. (15) induced unilateral emphysema in dogs by using repeated intrabronchial instillations of papain and performed isolated, bilateral stimulation of the phrenic nerves several months later. Phrenic nerve stimulation generated lower ΔPao’s in the emphysematous lung than in the intact, nonemphysematous lung. However, using sonomicrometry to measure diaphragm muscle length, Hubmayr et al. (15) found no difference between the two halves of the muscle during stimulation. Also, they did not evaluate the radii of muscle curvature, and they found no interhemidiaphragmatic differences in fiber-type distribution, fiber cross-sectional area, or maximal isometric tetanic tension in vitro. The mechanism of the interpulmonary difference in ΔPao, therefore, was not readily identified.

In the present study, the hypothesis was tested that the interpulmonary difference in ΔPao observed in dogs with experimental unilateral emphysema was primarily the result of a different shortening of the two halves of the diaphragm. Gradual, single-lung inflation was performed to simulate unilateral emphysema, and the phrenic nerves were bilaterally stimulated after the animals were placed in a computed tomographic (CT) scanner. As radiopaque markers were attached along muscle fibers in the midcostal region of the right and left hemidiaphragms, accurate measurements of muscle displacement, muscle length, and muscle curvature were obtained, and the changes in pressure generated in the two lungs were analyzed as functions of these parameters.

METHODS

The studies were carried out on six adult bred-for-research dogs (16–25 kg) anesthetized with pentobarbital sodium (initial dose, 30 mg/kg iv), as approved by the Animal Ethics and Welfare Committee of the Brussels School of Medicine. The animals were placed in the supine position and intubated with a cuffed endotracheal tube, and a venous cannula was inserted in the forelimb to give maintenance doses of anesthetic. A tracheostomy was performed through a midline incision of the neck, and two endotracheal tubes (n = 5–7) were inserted in the right and left main stem bronchi. The two tubes were positioned under endoscopic guidance to ensure patency of all
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lobar bronchi, after which they were tethered to the tracheal rings above and below the site of tracheostomy to avoid any inadvertent displacement later. After this procedure was completed, the C5 and C6 phrenic nerve roots were isolated bilaterally, and the abdomen was opened by a midline incision from the xiphisternum to the umbilicus. Rows of five polyethylene spheres were then stitched superficially to a muscle bundle in the midcostal region of both the left and the right hemidiaphragm, using the same method that has been previously described in detail (9, 20). A balloon-catheter system filled with 1.0 ml of air was also placed between the liver and the stomach to measure abdominal pressure (Pab).

After the abdomen was closely sutured, the animal was transferred to a V-shaped board and placed in a four-channel multidetector CT scanner (Somatom Volume Zoom 4, Siemens Medical Solutions, Forchheim, Germany). The C5 and C6 phrenic nerve roots were laid over two pairs of insulated stainless steel stimulating electrodes, and a differential pressure transducer (Validyne, Northridge, CA) was connected to a side port of each endobronchial tube to measure ΔPao in the two lungs separately. The animal was then made anemic by mechanical ventilation, and a first helical data acquisition starting at 5 cm caudal to the lower rib cage margin and extending to −2 cm cranial to the xiphoid process was performed during relaxation at FRC. The scanning parameters were similar to those used in previous studies (7, 9): 120 kV, 120 effective mA, 0.5 s per revolution scanning time, 1 mm collimation, and 6.9 mm feed/rotation. The animal was subsequently reconnected to the ventilator, after which the right lung (3 animals) or the left lung (3 animals) was passively inflated. In each animal, transrespiratory pressure in the inflated lung was increased by 7.5 cmH2O increments to ~30 cmH2O; once the target pressure was established, the two endobronchial tubes were occluded and a CT data acquisition was performed. After this procedure was completed, square pulses of 0.1-ms duration and supramaximal voltage were applied at a frequency of 20 impulses/s to the left and right phrenic nerve roots, first with both lungs at FRC, then after inflation of the right or left lung at the different transrespiratory pressures, and a new set of CT data acquisitions was obtained. All phrenic nerve stimulations were also performed while the animal was anemic and the two endobronchial tubes were occluded.

The animals were maintained at a constant, rather deep level of anesthesia throughout the study. Thus at no time in the experiment did they have a corneal reflex or movements of the fore- or hindlimbs. Rectal temperature was maintained constant between 36 and 38°C with infrared lamps. At the conclusion of the experiment, the animal was given an overdose of anesthetic (30–40 mg/kg iv).

Data analysis. Analysis of the CT data was made as previously described (9, 20). Thus, for each lung volume in each animal, 1.25-mm-thick transverse CT sections during relaxation and during phrenic nerve stimulation were reconstructed at 1.0 mm intervals by using a 360° linear-interpolation algorithm and a standard kernel (AB 40 f, Siemens Medical Solutions). Sagittal and coronal images were also reconstructed, and these multiplanar reconstructions were used in a workstation (Leonardo, Siemens Medical Solutions) to define the three-dimensional coordinates of each diaphragm marker and to measure the length of each hemidiaphragm. Particular attention was given to the markers situated near the central tendon. By convention, the coordinates of these markers along the craniocaudal and laterolateral axes were expressed in millimeters relative to their relaxed FRC position; a negative sign indicates, respectively, a caudal or medial displacement of the markers relative to that position. The length of each hemidiaphragm was also expressed in millimeters. To allow comparison between the two hemidiaphragms in the different animals, however, muscle lengths during relaxation and during phrenic nerve stimulation at the different lung volumes were then expressed as percentages of muscle length during relaxation at FRC (Lp/FRC).

The CT images were also used to measure the curvature of the two hemidiaphragms during phrenic stimulation. This was done in two steps, as previously described (7). First, for each hemidiaphragm at each lung volume, a 5-mm-thick plane was fit to the five markers in the row. Because of the striking contrast between air in the lung and the abdominal contents, the contour of the lung-apposed portion of the hemidiaphragm was clearly apparent, and this contour was traced from the rib cage to the marker situated near the central tendon. Then two chords of equal length were constructed in the contour, and normals to the chords were constructed at midchord points. The radius of curvature of the hemidiaphragm was measured from the intersection of the normals.

Statistical analysis. Data of ΔPao, ΔPab, position of the markers, diaphragm muscle length, and radius of curvature were averaged over the animal group, and they are presented as means ± SE. Statistical assessments of the effects of lung volume on the ΔPao values recorded in the inflated and noninflated lungs, on ΔPab, on muscle length and curvature in the ipsilateral and contralateral hemidiaphragms, and on the position of the markers situated near the central tendon, were made by analysis of variance (ANOVA) with repeated measures, and multiple comparison testing of the mean values was performed, when appropriate, using Student-Newman-Keul’s tests. Statistical comparisons between the inflated and noninflated lungs and between the ipsilateral and contralateral hemidiaphragms were made similarly. The criterion for statistical significance was taken as P < 0.05.

RESULTS

Pressure. Although the values of ΔPao recorded during phrenic nerve stimulation at FRC showed a large variation among the six animals, ranging from −21.0 to −46.0 cmH2O, the values in the right and left lungs were similar (right, −31.1 ± 3.2 cmH2O; left, −30.5 ± 3.7 cmH2O). With gradual inflation of the left or the right lung, however, ΔPao in the inflated lung decreased markedly in every animal, whereas in the noninflated lung, ΔPao remained nearly unaltered in two animals. Also, in the four animals that showed a decrease in ΔPao in both lungs, the magnitude of the decrease was consistently larger in the inflated lung than in the noninflated lung. As shown in Fig. 1, therefore, as transrespiratory pressure in the inflated lung increased for the six animals from 0 to 28.3 ± 0.6 cmH2O, ΔPao in this lung decreased from −30.5 ± 3.5 to −7.0 ± 1.3 cmH2O (P < 0.001), and ΔPao in the noninflated lung only decreased from −31.1 ± 3.5 to −24.8 ± 2.3 cmH2O (P < 0.01). The rise in Pab during stimulation also decreased with single-lung inflation from +12.2 ± 1.4 to +8.3 ± 1.3 cmH2O (P < 0.001).

Position and length of the relaxed diaphragm. The anterior-posterior view of the diaphragm markers during relaxation with both lungs at FRC and during relaxation after inflation of the left lung with a transrespiratory pressure of +31 cmH2O is shown for a representative animal in Fig. 2, and the craniocaudal (axial) and coronal position of the markers situated on both sides of the central tendon during relaxation at all lung volumes is shown for the six animals in Fig. 3. With the animal relaxed, the markers on both sides of the central tendon were progressively displaced in the caudal direction as lung volume increased (P < 0.001 for both sides). However, whereas the markers on the inflated side moved by 20.3 ± 1.3 mm as transrespiratory pressure on that side increased to +29.1 ± 1.2 cmH2O, the markers on the noninflated side moved by only 6.2 ± 1.6 mm (P < 0.001) (Fig. 3A). Concomitantly, the markers on the inflated side moved medially, toward the sagittal midplane, by 15.2 ± 1.9 mm (P < 0.001), whereas...
the markers on the noninflated side moved 10.6 ± 1.3 mm laterally, away from the sagittal midplane (P < 0.001) (Fig. 3B). On the other hand, the markers situated near the muscle insertions into the ribs on either side essentially remained stationary with increasing lung volume; the only significant displacement was a 3.8 ± 0.5 mm lateral displacement of the markers on the noninflated side (Fig. 2).

As a result of these displacements, both relaxed hemidiaphragms shortened with single-lung inflation (P < 0.01 for both), but the hemidiaphragm on the inflated side shortened more than that on the noninflated side (Fig. 4). Specifically, as transrespiratory pressure in the inflated lung increased to +29.1 cmH₂O, the ipsilateral hemidiaphragm shortened to 84.7 ± 1.7% of L_{FRC}, whereas the contralateral hemidiaphragm shortened only to 95.8 ± 1.8% of L_{FRC} (P < 0.001).

Position and length of the diaphragm during phrenic stimulation. The values of muscle length obtained for the two hemidiaphragms during phrenic nerve stimulation at all lung volumes are also shown in Fig. 4. During stimulation with both lungs at FRC, the muscle fibers in the right and left hemidiaphragms shortened equally to 57.0 ± 1.8% of L_{FRC}. After single-lung inflation, however, muscle length in the two hemidiaphragms decreased progressively as lung volume increased (P < 0.01 for both), but muscle length on the inflated side decreased more than that on the noninflated side (P < 0.01 or less). As a result, during stimulation at 28.3 cmH₂O, muscle length on the noninflated side was 54.4 ± 1.2% of L_{FRC}, whereas muscle length on the inflated side was only 51.4 ± 1.5% of L_{FRC}.

This interhemidiaphragmatic difference in muscle length during phrenic nerve stimulation was smaller than that during relaxation. In other words, in the presence of single-lung inflation, the amount of diaphragm shortening produced on the inflated side by phrenic stimulation was smaller than the amount of diaphragm shortening on the noninflated side, and the magnitude of the caudal displacement of the dome was also smaller, as shown in Fig. 2. Thus, for the six animals, the domes of the two hemidiaphragms moved equally by 45.5 ± 1.6 mm during stimulation at FRC, but during stimulation at 28.3 cmH₂O, the dome on the inflated side moved by 29.2 ± 2.3 mm, whereas the dome on the noninflated side still moved by 41.5 ± 1.2 mm (P < 0.001).

Radius of curvature. Figure 5 shows the computed radii of curvature for the two hemidiaphragms during phrenic nerve stimulation in the different conditions. In agreement with the previous measurements of Kim et al. (19) and Boriek et al. (1) and with our own measurements (7, 20), the radius of curvature in both hemidiaphragms was 26 to 45 mm during stimulation at FRC. With gradual, single-lung inflation, the radius of curvature of the ipsilateral hemidiaphragm increased progressively to 59.0 ± 7.6 mm (P < 0.001). In contrast, the radius of curvature of the contralateral hemidiaphragm remained unchanged.

Relationship between radius of curvature and muscle length. The values of radius of curvature for the two hemidiaphragms are plotted against the corresponding values of muscle length in Fig. 6. The data for the two hemidiaphragms appear to lie along a single line. Thus the radius of curvature was nearly
constant at 32–34 mm as muscle length ranged from 58 to 54% of LFRC. As muscle length in the ipsilateral hemidiaphragm decreased to 53.5% of LFRC, however, the radius increased sharply to 41 mm, and this trend continued as the length of the muscle decreased further.

**DISCUSSION**

The main findings of the study are that 1) with unilateral lung inflation, the pressure developed by the diaphragm in the inflated lung decreases markedly as lung volume increases, and the lung-inflating action of the muscle becomes very asymmetric; 2) the ipsilateral hemidiaphragm is displaced caudally and medially, so that the muscle is shorter than the contralateral hemidiaphragm both during relaxation and during bilateral phrenic nerve stimulation; and 3) the radius of curvature of the ipsilateral hemidiaphragm during stimulation is also greater than that of the contralateral hemidiaphragm. In the following sections, we will first compare these results with those reported by Hubmayr et al. (15) in dogs with experimental unilateral emphysema. We will then show that the changes in diaphragm length and curvature account well for the asymmetry of diaphragm function, and, finally, we will discuss the implications of these findings to the mechanics of the chest wall and to SLT in patients with emphysema.

**Comparison with previous studies.** When our animals had one lung inflated to a transrespiratory pressure of ~30 cmH₂O, the ΔPao developed in this lung during bilateral phrenic nerve stimulation was reduced to 7.0 cmH₂O or 24.0% of the control FRC value, whereas ΔPao in the contralateral, noninflated lung was relatively preserved and remained at 24.8 cmH₂O or 82% of the control value (Fig. 1). Because these ΔPao values were obtained with no airflow, they represent the mean ΔPpl values for each of the two lungs. These results, therefore, confirm the observation by Hubmayr et al. (15) that in the presence of unilateral lung inflation, the lung-expanding action of the diaphragm becomes asymmetric. The interpulmonary difference in ΔPao (and ΔPpl) measured in the present study was, in fact, much larger than that reported by these investigators; the
difference in that study was only 4 cmH$_2$O when the frequency of phrenic nerve stimulation was 20 Hz and 6 cmH$_2$O when the frequency was 50 Hz.

This quantitative difference cannot be attributed to a difference in the magnitude of lung inflation. Indeed, in the study by Hubmayr et al. (15), the volume of the emphysematous lung was two- to threefold that of the intact lung, so the interpulmonary difference in lung volume must have been close to that induced by full inflation in our animals. On the other hand, single-lung inflation in the present study was performed over a few seconds, whereas unilateral emphysema in Hubmayr et al.’s study was allowed to develop over 6–8 mo, and studies of limb muscles in mice and cats have clearly established that chronic muscle shortening induces a loss of sarcomeres in series along the muscle fibers (26, 27). A similar remodeling has been shown in the diaphragm of emphysematous hamsters (13, 18), and the result is that the length of individual sarcomeres is virtually restored to its initial value. Consequently, the possibility exists that in dogs with unilateral emphysema, the adverse effect of muscle length on the force developed by the hemidiaphragm on the affected side was partly offset by the smaller number of sarcomeres. This possibility, however, cannot be demonstrated at this stage as Hubmayr et al. (15) did not measure sarcomere length and number in the two halves of the diaphragm.

**Determinants of the asymmetrical action of the diaphragm in acute, single-lung inflation.** With passive, single-lung inflation, the rise in Ppl over the inflated lung causes a caudal displacement of the ipsilateral hemidiaphragm and a shift of the mediastinum toward the opposite side. Therefore, Ppl over the contralateral, noninflated lung should also rise, and the contralateral hemidiaphragm should also be displaced caudally. However, direct and indirect measurements of Ppl in dogs have shown that, when the airway of one lung is occluded and the other lung is passively inflated, the pressure rise over the noninflated lung is, on average, 70% of the pressure rise over the inflated lung (16). In the present study, as the airway of the noninflated lung was occluded after, rather than before inflation, the rise in Ppl over the noninflated lung should be an even smaller fraction of that over the inflated lung. Moreover, the caudal displacement of the ipsilateral hemidiaphragm leads to a rise in Pab, which should oppose the caudal displacement of the contralateral hemidiaphragm. On this basis, we predicted that passive, single-lung inflation would induce shortening of both hemidiaphragms, but that the amount of shortening on the inflated side would be greater than that on the noninflated side (8, 10). The present CT measurements confirmed the prediction in all respects. As is shown in Figs. 2–4, single-lung inflation caused a caudal displacement and shortening of both hemidiaphragms, and although the central tendon was shifted toward the contralateral side (this should attenuate the shortening of the ipsilateral hemidiaphragm and enhance the shortening of the contralateral hemidiaphragm), the displacement and shortening of the ipsilateral hemidiaphragm was more than threefold that of the contralateral hemidiaphragm.

As the muscle fibers of the diaphragm are activated and shorten, the dome descends, Ppl decreases, and Pab increases, and at equilibrium, the pressure generated by the diaphragm balances the load imposed on the muscle by Ppl and Pab (9, 10, 28). After passive, single-lung inflation, the ipsilateral hemidiaphragm lies caudal to the contralateral hemidiaphragm. Therefore, if the two hemidiaphragms were to reach the same axial position with phrenic nerve stimulation, the volume swept by the contralateral hemidiaphragm, and although the central tendon was shifted toward the contralateral side (this should attenuate the shortening of the ipsilateral hemidiaphragm and enhance the shortening of the contralateral hemidiaphragm), the displacement and shortening of the ipsilateral hemidiaphragm was more than threefold that of the contralateral hemidiaphragm. This difference in active muscle length between the two hemidiaphragms might appear small. However, it is well established that the relationship between the pressure developed by the diaphragm during phrenic nerve stimulation and muscle length is very steep when muscle length decreases to 60% of LFRC and below (9, 10, 17). In our previous study (9) for example, we found that, when the phrenic nerves were maximally stimulated at TLC, the diaphragm shortened to ~60% of LFRC and ∆Pao was approximately −35.0 cmH$_2$O. However, when the same stimulation was delivered with both lungs at TLC, muscle length at equilibrium was ~51% of LFRC, but ∆Pao was only ~3.0 cmH$_2$O. Thus, as lung volume increased from FRC to TLC and active diaphragm length decreased from 60 to 51% of LFRC, the ∆Pao generated by the diaphragm decreased by a factor of ~12. The current finding that in the presence of a full, single-lung inflation, the ∆Pao developed in the noninflated lung exceeded that in the inflated lung by a
factor of 3 is, therefore, fully consistent with the difference in active muscle length measured between the two halves of the diaphragm.

In an attempt to explain the strong dependence on muscle length of the pressure developed by the diaphragm at short muscle lengths, Boriek et al. (1) measured both the changes in length and the changes in curvature of the canine diaphragm during spontaneous inspiratory efforts and during phrenic nerve stimulation in the presence of bilateral lung inflation. They showed that the radius of muscle curvature remained nearly constant when muscle length decreased to 85–60% of L_{FRC}, but that it increased sharply when muscle length decreased further to 60–50% of L_{FRC}. These investigators also explained the changes in curvature by a simple geometric model in which the diaphragm is pictured as a circular arc that extends between the attachments on opposite sides of the rib cage, and they concluded that the radius of diaphragm curvature is, in fact, a function of muscle length (1). In agreement with these observations, during phrenic stimulation at 28.0 cmH_2O in our animals, the radius of curvature of the ipsilateral hemidiaphragm was nearly twofold that of the contralateral hemidiaphragm (Fig. 5). Furthermore, the data of radius of curvature and muscle length for the two hemidiaphragms appeared to fit a single relationship (Fig. 6), the shape of which was similar to that reported by Boriek et al. (1). This observation, in agreement with our hypothesis, further supports the view that in the presence of single-lung inflation, the asymmetrical action of the diaphragm on the two lungs is primarily determined by the differential effect of inflation on the length and curvature of the two hemidiaphragms.

Physiological implications. The present findings have two important physiological implications. First, they fully confirm our previous observation (6, 8) that the canine mediastinum, although delicate (12), can sustain significant transmural pressure. Specifically, based on 1) the interpulmonary difference in ΔPao observed during phrenic stimulation, and 2) the assumption that the rise in Ppl over the noninflated lung during passive inflation was ~40% of that over the inflated lung (see above), one can infer that, during phrenic stimulation in the presence of a full, single-lung inflation, the mean Ppl over the inflated lung was 20–25 cmH_2O more positive than that over the noninflated lung.

The second implication concerns the tension in the diaphragm muscle fibers. Because tension in the fibers is related to the product of pressure and radius of curvature, the differences observed between the ipsilateral and the contralateral hemidiaphragm in our animals imply that muscle tension on the noninflated side was greater than that on the inflated side, and this leads to the question as to what prevents tension in the contralateral hemidiaphragm from being transmitted to the ipsilateral hemidiaphragm.

The answer to the question is uncertain, but we speculate that the mediastinum plays a major role in this phenomenon. Thus, although the force exerted by the canine mediastinum on the diaphragm is small during phrenic nerve stimulation at FRC, this force represents a significant fraction of the force developed by the diaphragm when phrenic stimulation is performed after both lungs have been inflated to near TLC (7). Inasmuch as single-lung inflation causes both a large descent of the dome on the inflated side and a shift of the central tendon toward the noninflated side (Fig. 2), it should cause stretching of the mediastinum, so it would be expected that the mediastinum in this condition would also apply a significant force on the diaphragm during contraction. In so doing, it might take on part of the tension developed in the muscle fibers of the contralateral hemidiaphragm and, thus, reduce transmission of this tension across the midline. The previous observation that, in the presence of single-lung inflation, the interpulmonary difference in ΔPao during spontaneous inspiratory efforts (i.e., during coordinated contraction of the diaphragm and inspiratory intercostals) is abolished after section of the ventral mediastinal pleura (8) strongly supports this idea. Indeed it is reasonable to assume that mediastinal section would also abolish the interpulmonary difference in ΔPao during isolated phrenic nerve stimulation. In this case, transdiaphragmatic pressure (Pdi) across the two hemidiaphragms would therefore be equal or nearly equal, so tension in the muscle fibers would be equal as well.

Implications to SLT for emphysema. As previously pointed out, single-lung inflation in our animals was performed over a few seconds, whereas in patients with SLT for emphysema, the asymmetry in diaphragm size develops slowly over several weeks or months and may induce remodeling in the muscle. Measurements of Pdi during phrenic nerve stimulation in patients with severe emphysema and hyperinflation have suggested, however, that in contrast to small quadrupeds, sarcromere adaptation in the human diaphragm is limited (24). Therefore, even though the present findings cannot be extended to humans without considerable caution, one would predict that in patients with emphysema, SLT would improve the pressure-generating capacity of the diaphragm on the transplanted side compared with the native side. If the assumption is also made that neural drive to the diaphragm remains symmetrical after the procedure, and some evidence has been provided in support of this assumption (2), then it would be expected that ΔPpl over the transplanted lung would be greater than that over the native lung during inspiration. The observation by radioisotope techniques that after SLT, expansion of the transplanted lung during resting breathing is much greater than expansion of the native lung (4, 14), is consistent with this prediction.

On the basis of the interpulmonary difference in ΔPpl, it would also be expected that inspiration in such patients would be associated with a shift of the mediastinum toward the transplanted lung. However, CT measurements in seven patients have shown that the mediastinum, in fact, shifts toward the native lung (5). This apparent discrepancy would therefore support the hypothesis of De Groote et al. (5) that the mediastinal shift observed in these patients is primarily the result of the increase in mediastinal tension induced by the caudal displacement of the diaphragm combined with the ventral displacement of the sternum.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).
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