The effect of lung inflation on the inspiratory action of the canine parasternal intercostals

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Leduc, Dimitri, and André De Troyer. The effect of lung inflation on the inspiratory action of the canine parasternal intercostals. J Appl Physiol 100: 858–863, 2006. First published November 17, 2005; doi:10.1152/japplphysiol.00739.2005.—Inflation induces a marked decrease in the lung-expanding ability of the diaphragm, but its effect on the parasternal intercostal muscles is uncertain. To assess this effect, the phrenic nerves and the external intercostals were severed in anesthetized, vagotomized dogs, such that the parasternal intercostals were the only muscles active during inspiration, and the endotracheal tube was occluded at different lung volumes. Although the inspiratory electromyographic activity recorded from the muscles was constant, the change in airway opening pressure decreased with inflation from $-7.2 \pm 0.6$ cmH\textsubscript{2}O at functional residual capacity to $-2.2 \pm 0.2$ cmH\textsubscript{2}O at 20 cmH\textsubscript{2}O transrespiratory pressure ($P < 0.001$). The inspiratory cranial displacement of the ribs remained virtually unchanged, and the inspiratory caudal displacement of the ribs decreased moderately. However, the inspiratory outward rib displacement decreased markedly and continuously; at 20 cmH\textsubscript{2}O, this displacement was only 23 $\pm$ 2% of the value at functional residual capacity. Calculations based on this alteration yielded substantial decreases in the change in airway opening pressure. It is concluded that, in the dog, 1) inflation affects adversely the lung-expanding actions of both the parasternal intercostals and the diaphragm; and 2) the adverse effect of inflation on the parasternal intercostals is primarily related to the alteration in the kinematics of the ribs. As a corollary, it is likely that hyperinflation also has a negative impact on the parasternal intercostals in patients with chronic obstructive pulmonary disease.

IT IS WELL ESTABLISHED, BOTH in humans (5, 10, 21, 38) and in animals (1, 11, 22), that the intercartilaginous portion of the internal intercostal muscles (the so-called parasternal intercostals) contracts in concert with the diaphragm during the inspiratory phase of the breathing cycle. In fact, in anesthetized dogs, these muscles play a predominant role in producing the elevation of the ribs and contribute significantly to the expansion of the lung (6, 17). It is also well established that inflation of the respiratory system from functional residual capacity (FRC) to total lung capacity (TLC) induces shortening of the diaphragm and thereby causes a marked decrease in the pressure-generating ability of the muscle (2, 26, 30, 32, 35). However, the effect of inflation on the pressure-generating ability of the parasternal intercostals remains uncertain.

In supine dogs, the resting length of the diaphragm at FRC is close to the in vitro optimal force-producing length of the muscle ($L_o$), but the resting FRC length of the parasternal intercostals is 10–15% longer than $L_o$ (19). As these muscles shorten by 5–10% during inflation from FRC to TLC (3, 14, 18, 34), they should, therefore, move toward $L_o$, rather than away from it. Indeed, in agreement with the length-tension characteristics of skeletal muscles, studies by Decramer and colleagues (4, 24) have shown that the canine parasternal intercostals generate a similar or slightly greater force on the ribs during isolated stimulation near TLC than during stimulation at TLC. Based on this finding, these investigators concluded that, with inflation, the mechanical effect of the parasternal intercostals was much better preserved than that of the diaphragm, and they further suggested that patients with chronic obstructive pulmonary disease and severe hyperinflation might benefit more from breathing exercises designed to train the rib cage muscles than from exercises designed to promote diaphragmatic breathing (24).

However, recent studies of the coupling between the ribs and the lung in dogs have shown that the fall in airway opening pressure ($\Delta P_{a o}$) induced by an external load applied to the ribs in the cranial direction decreases markedly with increasing lung volume (12). In addition, these studies have also shown that this volume effect on $\Delta P_{a o}$ is primarily the result of the kinematics of the ribs. Thus the ribs in the dog are slanted caudally at FRC and move through a rotation around the axis defined by their vertebral articulations (29). Consequently, as the ribs rotate cranially with inflation, they become oriented more transversely relative to the sagittal midplane, and, hence, a given cranial rib displacement leads to a smaller outward displacement and a smaller lung expansion. Although inflation may enhance the force-producing ability of the parasternal intercostals (4, 24), it would therefore be expected that it would have a detrimental effect on the lung-expanding action of these muscles. The present studies were undertaken to test this hypothesis.

METHODS

The studies were carried out on nine adult cross-breed dogs (12–21 kg body wt) 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 posture and intubated with a cuffed endotracheal tube, and a venous cannula was inserted in the forelimb to give maintenance doses of anesthetic (3–5 mg·kg\textsuperscript{-1}·h\textsuperscript{-1} iv). The abdomen was then opened by a midline incision from the xiphisternum to the umbilicus, and a balloon-catheter system was positioned between the liver and the stomach to measure abdominal pressure (Pab); the balloon was filled with 1.0 ml of air. After the abdomen was closely sutured, the

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vagi were isolated through a midline incision of the neck, infiltrated with 2% lidocaine (lignocaine), and sectioned. The C3, C5, and C7 phrenic nerve roots were also isolated bilaterally and sectioned so as to induce a complete paralysis of the diaphragm, after which the rib cage and intercostal muscles were exposed on both sides of the chest from the first to the tenth rib by reflection of the skin and superficial muscles, including the prominent medial head (pars supracostalis) of the scalene. The external intercostals and levator costae in all interspaces from the first to the seventh were subsequently sectioned from the costochondral junctions to the spine.

Measurements. The craniocaudal (axial) and lateral displacements of the ribs were measured by using linear displacement transducers (Schaevitz Engineering, Pennsauken, NJ), as previously described (11). In each animal, a hook was thus screwed into the fourth or the fifth rib in the midaxillary line and connected, through long inextensible threads, to two displacement transducers. One thread was led caudally, parallel to the longitudinal body axis of the animal, to a transducer placed at the foot of the table, and the second thread was led laterally, perpendicular to the sagittal midplane of the body, to a transducer placed at the side of the animal. A hook was also screwed into the sternum and connected to an additional displacement transducer placed at the foot of the table to measure the axial displacement of the sternum.

Pao was measured with a differential pressure transducer (Validyne, Northridge, CA) connected to a side port of the endotracheal tube, and the electromyogram (EMG) of the parasternal intercostals in the third interspace was recorded with a pair of stainless steel hook electrodes spaced 3–4 mm apart. These electrodes were placed in parallel fibers and inserted in the muscle bundles near the sternum, i.e., in the area of the muscle that receives the greatest inspiratory drive (13, 28). In four animals, similar pairs of hook electrodes were also inserted in the ventral head of the scalene muscle, in the sternomastoid, and in the dorsal portion of the external intercostals in the eighth and ninth interspaces, immediately ventral to the rib angle. All EMG signals were processed with amplifiers (CWE, model 830/1, Ardmore, PA) and bandpass filtered <100 and >2,000 Hz; the EMG signal from the parasternal intercostal was also rectified before its passage through a leaky integrator with a time constant of 0.2 s.

Protocol. The animal was allowed to recover for 30 min after instrumentation, after which Pao, Pab, rib and sternum motion, and EMG activity were recorded. The animal was breathing spontaneously throughout. Every 5–10 breaths, however, a syringe was connected to the endotracheal tube, and lung volume was increased above FRC, at which time the tube was occluded. The inflation was always performed during the expiratory pause, and the occlusion was maintained for a single inspiratory effort. We could, therefore, assess the pressure-generating ability of the parasternal intercostal muscles over a wide range of lung volumes without any significant change in chemical respiratory drive. At least 20–40 different levels of inflation taken in random order were applied in each animal; four to six occluded breaths were also obtained at FRC.

The animals appeared to remain at a satisfactory depth of anesthesia throughout. They did not react to painful stimuli and made no spontaneous movements other than respiratory movements, both during surgery and during the measurements. Also, they had no pupillary light reflex and no corneal reflex, thus indicating a deep level of anesthesia. Rectal temperature was kept constant between 36 and 38°C with infrared lamps. At the end of the experiment, the animals were given an overdose (30–40 mg/kg iv) of anesthetic, and postmortem examination of the rib cage was performed. In two animals, a few deep muscle bundles remained apparently intact in the most dorsal portion of the external intercostal and levator costae in the first and second interspaces. In seven animals, however, the muscles in interspaces 1–7 on both sides of the chest were completely sectioned.

Data analysis. Phasic inspiratory electrical activity in the parasternal intercostal muscle during each occluded breath in each individual animal was quantified by measuring the peak height of the integrated EMG signal in arbitrary units, and the inspiratory changes in Pao and Pab and inspiratory displacements of the ribs and sternum were measured relative to the onset of the parasternal inspiratory burst. Consequently, the pressures and displacements that were considered in the study’s calculations resulted exclusively from the contraction of inspiratory muscles and were not corrupted by the relaxation of the expiratory muscles at the end of expiration (15). By convention, inspiratory displacements in the cranial or outward direction were given positive signs, and inspiratory displacements in the caudal or inward direction were given negative signs. Electrical activity in the parasternal intercostal, the ΔPao and ΔPab, and the rib and sternum displacements measured during the occluded breaths at the different lung volumes were then plotted against the value of Pao before inspiration (i.e., the precontractile transrespiratory pressure), and lines of best fit were drawn by eye through all trials. Pressures and displacements at fixed transrespiratory pressures at 2.5 cmH2O increments were determined from these lines by interpolation.

Data were finally averaged over the animal group, and they are presented as means ± SE. Statistical assessments of the effects of lung volume were made by ANOVA with repeated measures, and multiple-comparison testing of the mean values was performed, when appropriate, using Student-Newman-Keuls tests. The criterion for statistical significance was taken as P < 0.05.

RESULTS

The records of Pao, Pab, and parasternal intercostal EMG activity obtained in a representative animal during an occluded breath at FRC and during an occluded breath at a higher lung volume are shown in Fig. 1, A and B, respectively, and Fig. 1C shows the pressure changes measured in the same animal during all trials at all lung volumes. During the occluded breath at FRC (Fig. 1A), ΔPao amounted to −8.0 cmH2O, and ΔPab was −4.0 cmH2O. In contrast, when lung volume before occlusion was increased to a transrespiratory pressure of 19 cmH2O (Fig. 1B), ΔPao and ΔPab were only −2.0 and −1.5 cmH2O, respectively. In fact, ΔPao and ΔPab decreased progressively as transrespiratory pressure was increased (Fig. 1C). The inspiratory EMG activity recorded from the parasternal intercostals during occlusion at high lung volumes, however, remained similar to that recorded during occlusion at FRC.

Inflation affected similarly the pressure changes in all animals (Fig. 2). As transrespiratory pressure was increased from 0 to 20 cmH2O, ΔPao for the animal group thus decreased from −7.2 ± 0.6 to −2.2 ± 0.2 cmH2O (P < 0.001), and ΔPab decreased from −3.1 ± 0.5 to −1.1 ± 0.2 cmH2O (P < 0.001). The inspiratory cranial displacement of the ribs during occlusion showed little or no change with inflation (Fig. 3). However, the inspiratory outward displacement of the ribs decreased continuously and markedly in every animal. Whereas this displacement at FRC averaged 3.2 ± 0.5 mm, at a transrespiratory pressure of 20 cmH2O, it was only 0.8 ± 0.2 mm (P < 0.001). In contrast to the cranial rib displacement, therefore, the outward rib displacement was closely related to ΔPao, as shown in Fig. 4.

The sternum moved caudally during inspiration at all lung volumes, and the magnitude of this displacement remained unchanged until transrespiratory pressure was increased to 12.5 cmH2O (Fig. 3). When transrespiratory pressure was increased further, however, sternum displacement decreased gradually (P < 0.001). The scalenes, the sternomastoids, and the external intercostals in the eighth and ninth interspaces did not show any inspiratory EMG activity in the four animals studied.

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DISCUSSION

The animals in this study had a complete paralysis of the diaphragm, and the external intercostal and levator costae muscles in interspaces 1–7 were severed on both sides of the chest. Also, in agreement with our previous observation that, in the dog, the neck muscles and the external intercostals in the most caudal interspaces have high thresholds of activation (7, 8), our animals did not have any inspiratory EMG activity in these muscles, including during occluded breaths at high lung volumes. The parasternal intercostals, therefore, were the only muscles active during inspiration. Furthermore, all measurements were made while the animals were breathing spontaneously. Consequently, the muscles contracted in all interspaces in a coordinated manner, and the normal spatial distribution of neural drive among them was maintained (13, 27, 28). In addition, the animals had a bilateral cervical vagotomy and showed no alteration in parasternal inspiratory EMG activity with increasing lung volume. To the extent that the action potential recorded from this muscle in response to a given twitch stimulation of the motor nerve is known to remain unchanged during passive inflation from FRC to TLC (34), such a lack of alteration in inspiratory EMG activity indicates that neural drive to the muscles was constant. Yet ΔPao and ΔPab decreased markedly and continuously with increasing lung volume in every animal of the study (Figs. 1 and 2). On the basis of these findings, the conclusion can, therefore, be drawn that, in the dog, inflation does adversely affect the lung-expanding action of the parasternal intercostals.

The magnitude of this adverse effect is compared with that for the diaphragm in Fig. 5. The solid circles in Fig. 5 indicate the ΔPao values measured during isolated contraction of the parasternal intercostals, with ΔPao expressed as a percentage of the FRC value, and the open circles indicate the ΔPao values obtained in similar dogs during isolated, tetanic stimulation of the C₅ and C₆ phrenic nerve roots in the neck (9). Also shown in Fig. 5 are the ΔPao values measured during the application of external loads to the second through seventh rib pairs in the cranial direction at 10- and 20-cmH₂O transrespiratory pres-
sure (crossed squares); such loading reproduces the pattern of rib displacement caused by isolated contraction of the external intercostals (12). It is apparent that, for a given increase in lung volume, the relative decrease in $P_{aO}$ for the parasternal intercostals is identical to that for external rib loading and only slightly smaller than that for the diaphragm. These findings confirm the previous observation by Ninane and Gorini (31) that, when the endotracheal tube is occluded in dogs and the parasternal intercostal in the third interspace is selectively activated by electrical stimulation at different lung volumes, $\Delta P_{ao}$ decreases as lung volume is increased. These investigators also reported that the cranial displacement of the ribs produced by contraction of the parasternal intercostal decreased with increasing lung volume and that the caudal displacement of the sternum increased. They concluded, therefore, that the adverse effect of inflation on the lung-expanding action of the parasternal intercostals is primarily related to the greater impedance of the ribs to cranial displacement. Furthermore, because a caudal displacement is expiratory in direction, they also implied that the greater caudal displacement of the sternum added to the reduction in cranial rib displacement and enhanced the decrease in $\Delta P_{ao}$.

**Fig. 3.** Mean ± SE values of axial (cranial) rib displacement, lateral (outward) rib displacement, and axial (caudal) sternum displacement obtained from 9 animals during isolated contraction of the parasternal intercostal muscles at different lung volumes.

**Fig. 4.** Relationships between $\Delta P_{ao}$ and the inspiratory displacement of the ribs in the cranial (A) and outward (B) directions during isolated contraction of the parasternal intercostal muscles at different lung volumes. Mean values were obtained from 9 animals. The numbers in both panels refer to the values of transrespiratory pressure before muscle contraction.

**Fig. 5.** Comparison between the effects of inflation on the pressure-generating ability of the parasternal intercostals and the diaphragm. The data shown for the parasternal intercostals (●) are the mean ± SE values of $\Delta P_{ao}$ obtained from 9 animals during isolated, spontaneous contraction of the muscles at different lung volumes (same data as in Fig. 2). The data shown for the diaphragm (○) are the mean ± SE values of $\Delta P_{ao}$ obtained from 7 animals during isolated, tetanic stimulation of the C5 and C6 phrenic nerve roots in the neck (from Ref. 9). The values of $\Delta P_{ao}$ are expressed as percentages of the FRC values to allow comparison between the two muscles. The two crossed squares at 10- and 20-cmH$_2$O transrespiratory pressure are the mean values obtained during external loading of the second through seventh rib pairs in the cranial direction (from Ref. 12).
However, when transrespiratory pressure in our animals was increased from 0 to 10 cmH₂O, the inspiratory cranial displacement of the ribs and inspiratory caudal displacement of the sternum remained unchanged (Fig. 3), thus suggesting that the force developed by the parasternal intercostals was essentially unaltered, and yet ΔPao decreased markedly to 57% of the FRC value. Also, when transrespiratory pressure was increased from 10 to 20 cmH₂O, the inspiratory caudal displacement of the sternum decreased, rather than increased, and ΔPao decreased further. It is unclear why the axial displacements of the ribs and sternum observed in the present study differed from those reported by Ninane and Gorini (31), but it is worth pointing out that, in the dog, axial rib and sternum displacements are linked, such that the inspiratory caudal displacement of the sternum reduces the cranial displacement of the ribs and vice versa (16, 17). The decrease in the caudal sternum displacement observed at high lung volumes in our animals, therefore, may help explain the maintenance of the cranial rib displacement. More importantly, such axial displacements indicate that these displacements are not the main determinants of the adverse effect of inflation on the lung-expanding action of the parasternal intercostals.

On the other hand, the inspiratory outward displacement of the ribs decreased continuously and markedly with increasing lung volume in every animal (Fig. 3). The outward rib displacement was also closely related to ΔPao (Fig. 4B), thus suggesting, in agreement with our initial hypothesis, that this alteration in rib displacement plays a major role in causing the detrimental effect of inflation on the lung-expanding action of the parasternal intercostals. In fact, the present data allow the role of this alteration to be estimated in a more quantitative manner. Thus, in the dog at FRC, the increase in lung volume per unit rib displacement is about four times greater for outward than for cranial rib displacement (17). If the ΔPao produced by an axial rib displacement of 1 mm is denoted \( a \), the cranial rib displacement is denoted \( X_r \), and the lateral rib displacement is denoted \( Y_r \), the relationship between rib displacement and ΔPao during contraction of the parasternal intercostals at a given lung volume can, therefore, be expressed, to a good approximation, by the following equation

\[
\Delta P_{ao} = a(X_r + 4Y_r) \quad (1)
\]

The values of cranial and outward rib displacement measured at any given transrespiratory pressure can then substitute for \( X_r \) and \( Y_r \), respectively, and the value of ΔPao thus calculated can be compared with that at FRC. As shown in Fig. 6, the computed values of ΔPao (open circles) decreased markedly and continuously with increasing transrespiratory pressure in much the same way as the measured values of ΔPao (solid circles) did.

The computed values of ΔPao were greater than the measured values at all transrespiratory pressures, and this suggests that the reduction in ΔPao during inflation involved an additional factor. There is a possibility that the ratio for the effectiveness of the outward over the cranial rib displacement does not remain constant but actually increases with increasing lung volume. If so, the computed values of ΔPao at high transrespiratory pressures would be smaller and the difference between the computed values and the measured values would also be smaller. To test the potential influence of this factor, we assumed that the ratio increased from 4 to 5 as transrespiratory pressure was increased from 0 to 20 cmH₂O. As shown in Fig. 6, the new computed ΔPao values (open squares) did fall below the initial values, but the difference relative to the measured values was essentially unchanged. Similarly, decreasing the ratio from 4 to 3 at high lung volumes had a relatively small effect on the computed ΔPao values (open triangles). On the other hand, it is well established that, in supine dogs, the diaphragm develops significant passive tension at FRC and that diaphragmatic compliance increases gradually with increasing lung volume (12, 23, 32, 33, 36). It would be expected, therefore, that, during isolated contraction of the parasternal intercostals at high lung volumes, a given fall in intrathoracic pressure would lead to a greater cranial (passive) displacement of the diaphragm and would induce a greater loss in ΔPao. As discussed in our previous communication (12), the magnitude of this loss cannot be assessed with precision. However, even if one assumes that the ratio for the effectiveness of the outward over the cranial rib displacement at high lung volumes is only 3 and that the difference between the computed and the measured values of ΔPao entirely results from the increase in diaphragmatic compliance, it appears that the effect of this factor on ΔPao is smaller than that of the reduced outward rib displacement, in particular at high lung volumes. Specifically, the increase in diaphragmatic compliance in this condition would still account for only 25% of the total reduction in ΔPao at 20-cmH₂O transrespiratory pressure, whereas the reduction in outward rib displacement would account for 75%.

In difficult to make a quantitative prediction of the effect of inflation on the parasternal intercostal muscles in humans, but the present observations have two implications. First, the bucket-handle rotation of the human ribs during passive inflation (39) is similar in magnitude to that observed in the dog
on the inspiratory intercostal muscles than on the diaphragm hyperinflation may actually have a greater detrimental effect in patients with severe chronic obstructive pulmonary disease, as a corollary, the speculation should be offered that, in the extent that the adverse effect of inflation on the parasternal intercostals would be primarily related to the kinematics of the ribs, it would also be expected that, in chronic inflation, a loss of sarcomeres in the muscles would cause little or no compensation. As a corollary, the speculation should be offered that, in patients with severe chronic obstructive pulmonary disease, hyperinflation may actually have a greater detrimental effect on the inspiratory intercostal muscles than on the diaphragm.

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