Mechanism of increased inspiratory rib elevation in ascites

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Leduc D, De Troyer A. Mechanism of increased inspiratory rib elevation in ascites. J Appl Physiol 107: 734–740, 2009. First published July 16, 2009; doi:10.1152/japplphysiol.00470.2009.—The detrimental effect of ascites on the lung-expanding action of the diaphragm is partly compensated for by an increase in the inspiratory elevation of the ribs, but the mechanism of this increase is uncertain. To identify this mechanism, the effect of ascites on the response of rib 4 to isolated phrenic nerve stimulation was first assessed in four dogs with bilateral pneumothoraces. Stimulation did not produce any axial displacement of the rib ($X_r$) in the control condition and caused a cranial rib displacement in the presence of ascites. This displacement, however, was small. In a second experiment, the effects of ascites on the pleural pressure swing ($\Delta P_{pl}$), intercostal activity, and $X_r$ during spontaneous inspiration were measured in eight animals. As the volume of ascites increased from 0 to 200 ml/kg body wt, $X_r$ increased from $3.5 \pm 0.5$ to $7.5 \pm 0.9$ mm ($P < 0.001$), $\Delta P_{pl}$ decreased from $-6.4 \pm 0.4$ to $-3.6 \pm 0.3$ cmH$_2$O ($P < 0.001$), and parasternal intercostal activity increased $61 \pm 19\%$ ($P < 0.001$). The role of the decrease in $\Delta P_{pl}$ in causing the increase in $X_r$ was then separated from that of the increase in intercostal muscle force using the relation between rib motion and $P_{pl}$. The loss in $\Delta P_{pl}$ accounted for two-thirds of the increase in $X_r$. These observations indicate that 1) the increased inspiratory elevation of the ribs in ascites is not the result of the increase in the rib cage-expanding action of the diaphragm and 2) it is due mostly to the decrease in $\Delta P_{pl}$ and partly to the increase in the force exerted by the parasternal intercostals on the ribs. These observations also suggest, however, that the rib cage expansion caused by ascites makes the parasternal intercostals less effective in pulling the ribs cranially.

Chest wall mechanics; respiratory muscles; diaphragm; intercostal muscles

Motivated by the common occurrence of dyspnea in ascites (1, 31, 32), we recently studied the mechanics of the canine diaphragm in the presence of increasing amounts of liquid in the peritoneal cavity. We showed that the liquid, by displacing the diaphragm cranially and the abdominal muscles outward, induces passive tension in both muscles (22, 24, 25) and causes an increase in the elastance of the abdominal compartment of the respiratory system (24). Consequently, the descent of the diaphragm occurring in response to a given activation is impeded. As a result, the muscle fibers during contraction are longer and develop greater force, but the lung-expanding action of the muscle is reduced (22, 24). Also, when the amount of liquid in the peritoneal cavity is large, the radius of curvature of the active diaphragm is increased, so that the inspiratory action of the muscle is further impaired (22). During spontaneous breathing in the dog, however, the adverse effect of ascites on the diaphragm is, in part, compensated for by an increase in the inspiratory elevation of the ribs and an increase in rib cage expansion (24). Although the pattern of chest wall motion in humans with ascites has not been investigated, an increase in inspiratory rib cage expansion has also been reported during pregnancy (16). The mechanism of this increase in inspiratory rib cage expansion, however, is uncertain.

Three mechanisms working alone or in combination might operate. First, because ascites causes both an increase in abdominal elastance and a cranial displacement of the diaphragm, one would expect that the so-called “insertional” and “appositional” forces of the muscle would be greater (12, 28). Therefore, a given diaphragmatic contraction should lead to a larger cranial displacement of the ribs. Second, even though the reduction in tidal volume observed in ascites is less than anticipated on the basis of the decrease in the lung-expanding action of the diaphragm, the decrease in minute ventilation elicits an increase in arterial Pa$_{CO_2}$ (24). As a result, the neural drive to the inspiratory muscles, in particular the parasternal intercostals, is increased, and the force exerted by the muscles on the ribs, tending to pull them cranially and outward, is greater (24). Finally, the fall in pleural pressure ($\Delta P_{pl}$) during inspiration, whether it is generated by the diaphragm or inspiratory intercostals, acts as a load on the ribs, and we (10) have recently shown that the decrease in $\Delta P_{pl}$ plays a dominant role in causing the increased inspiratory rib elevation after the induction of a diaphragmatic paralysis. As tidal volume decreases with ascites, one would therefore predict that $\Delta P_{pl}$ also decreases, leading to an increase in rib elevation independent of any change in diaphragmatic action on the ribs or any increase in intercostal activity.

The present study was designed to assess the role played by these three mechanisms in determining the increase in inspiratory rib elevation in ascites. Two sets of experiments were performed in dogs. In the first set, we examined the response of the ribs to isolated phrenic nerve stimulation in the presence of increasing amounts of liquid in the abdominal cavity. As the animals had bilateral pneumothoraces, the confounding influence of the changes in $\Delta P_{pl}$ on rib motion was eliminated, and the observed alterations were exclusively related to the action of the diaphragm on the rib cage. In the second set of experiments, we measured the effects of ascites on $\Delta P_{pl}$, intercostal muscle activity, and rib motion during spontaneous breathing, and the role of $\Delta P_{pl}$ was separated from that of intercostal muscle force using the relation between rib motion and $\Delta P_{pl}$ during passive lung inflation.

METHODS

Experiments were carried out on 12 adult cross-breed dogs (19–40 kg body wt) anesthetized with pentobarbital sodium (initial dose: 30 mg/kg iv) as approved by the Animals Ethics and Welfare Committee of the Brussels School of Medicine. Animals were placed in the...
supine posture and intubated with a cuffed endotracheal tube, and a venous canula was inserted in the forelimb to give maintenance doses of anesthetic. The abdomen was opened by a 3- to 4-cm-long midline incision, and a balloon-catheter system filled with 1.0 ml air was placed between the stomach and liver to measure the changes in abdominal pressure ($\Delta P_{ab}$). A catheter was also inserted through the right external oblique and internal oblique muscles of the abdomen, midway between the iliac crest and the costal margin, such that liquid could easily be introduced into the abdominal cavity later. After the abdomen was closely sutured, the rib cage and intercostal muscles were exposed on both sides of the chest from the first to the ninth rib by reflection of the skin and superficial muscle layers, and a hook was screwed into the fourth rib in the midaxillary line and connected to a linear displacement transducer (Schaevitz Engineering, Pennington, NJ) to measure the craniocaudal (axial) displacement of the rib ($X_r$), as previously described (8). Two experimental protocols were then followed.

**Experiment 1.** Four animals were studied first to assess the effect of ascites on the action of the diaphragm on the ribs independent of the alterations in $\Delta P_{pl}$ that ascites would induce otherwise. Thus, in each animal, the C5 phrenic nerve roots were isolated in the neck and laid over two pairs of insulated stainless steel stimulating electrodes. The animal was then connected to a mechanical ventilator (Harvard Pump, Chicago, IL), and the intercostal muscles in the second interspace were severed over ~2 cm to induce a bilateral pneumothorax. After the animal was hyperventilated to apnea, $\Delta P_{ab}$ and $X_r$ were measured while square pulses of 0.1-ms duration and supramaximal voltage (7) were applied at a frequency of 20 impulses/s to the phrenic nerve roots. Two trials of stimulation were performed, after which a volume of isosmotic liquid (1.36% Dianeal glucose, Baxter) corresponding to 50 ml/kg body wt was introduced into the abdominal cavity. Liquid volume was subsequently increased by increments of 50 ml/kg body wt to a total of 200 ml/kg. As during control, two runs of resting breathing were obtained in each condition. In five animals, the relationship between $X_r$ and $P_{pl}$ during passive inflation was also assessed as the volume of ascites was gradually increased.

**Animals in experiment 1** were maintained at a constant, rather deep, level of anesthesia throughout. They had no corneal reflex and no movements of the forelimbs or hindlimbs, including during phrenic nerve stimulation. In contrast, to avoid obscuring the response studied, we regulated the anesthesia in experiment 2 to keep the corneal reflex present throughout the measurements. Rectal temperature in these animals was also maintained constant between 36 and 38°C with infrared lamps. At the end of the experiment, the animal was given an overdose of anesthetic (30–40 mg/kg iv).

**Data analysis.** For each volume of ascites in each animal of experiment 1, the values of $\Delta P_{ab}$ and $X_r$ obtained during phrenic stimulation were averaged over the two trials. By convention, $X_r$ was considered negative when the rib moved caudally and positive when it moved cranially.

![Fig. 1. Axial displacements of the fourth rib ($X_r$) and changes in abdominal pressure ($\Delta P_{ab}$) obtained during tetanic stimulation of the C5 phrenic nerve roots in the presence of increasing ascites. Values are means ± SE from 4 animals with bilateral pneumothorax. Positive values for $X_r$ indicate cranial displacements. *$P < 0.01$ and **$P < 0.001$ for ascites vs. control.](http://jap.physiology.org/)

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The evaluation of the role played by $P_{pl}$ in causing the increase in inspiratory rib elevation in the presence of ascites (experiment 2) was made in two stages, as previously described (10). First, for each volume of ascites in each individual animal, $\Delta P_{pl}$, $\Delta P_{ab}$, $X_r$, and phasic inspiratory EMG activity in the parasternal and external intercostals were averaged over 10 consecutive breaths from each run. Inspiratory EMG activity in each muscle was first quantified by measuring the peak height of the integrated EMG signal in arbitrary units, and it was then expressed as a percentage of the activity recorded before ascites (control). The parasternal intercostal EMG signal was also used as a marker of inspiration and, therefore, as a time reference for the inspiratory rib displacement upward), changes in pleural pressure ($P_{pl}$) and $P_{ab}$, and parasternal and external intercostal EMG activity (integrated signals) obtained from a representative animal during spontaneous breathing in the control condition to compute the increase in $X_r$ attributable to the pressure loss, and $\Delta P_{pl}$ was then multiplied by the loss in $P_{pl}$ observed during breathing with this particular volume to yield the increase in $X_r$ attributable to the pressure loss, and this increase was then added to the $X_r$ measured during breathing in the control condition to compute the $X_r$ that would be observed during ascites if the loss in $\Delta P_{pl}$ were the only operating factor. The values of $X_r$ thus predicted for all volumes of ascites in the eight animals are compared with the measured values in Fig. 5. Although the predicted values are lower than the measured values at all volumes from 100 to 200

**Experiment 2.** The records of $X_r$, $\Delta P_{pl}$, $\Delta P_{ab}$, and intercostal EMG activity obtained in a representative animal during spontaneous breathing in the control condition and in the presence of 150 ml/kg ascites are shown in Fig. 2, and the values obtained for the different volumes of ascites in the eight animals are shown in Fig. 3. $X_r$ remained unaltered when ascites was 50 ml/kg, but it increased progressively as ascites increased from 50 to 200 ml/kg ($P < 0.001$; Fig. 3A). For the animal group, therefore, whereas $X_r$ during control was 3.47 ± 0.52 mm, with 200 ml/kg ascites it was 7.47 ± 0.89 mm. At the same time, $\Delta P_{pl}$ decreased gradually from $-6.40 \pm 0.37$ to $-3.61 \pm 0.32 \text{cmH}_2\text{O}$ ($P < 0.001$; Fig. 3B), whereas $\Delta P_{ab}$ did not show any significant change (Fig. 3C). The inspiratory EMG activity recorded from the external intercostal muscles did not show any significant change either, but the activity recorded from the parasternal intercostals increased progressively ($P < 0.001$). With 200 ml/kg ascites, the peak height of the integrated EMG signal thus amounted to 161.1 ± 18.8% of the control value.

During passive inflation, the rise in $P_{pl}$ and cranial rib displacement obtained for a given increase in lung volume increased progressively as ascites increased, but the ratio of $X_r$ to $\Delta P_{pl}$ remained essentially unchanged, independent of the volume of ascites (Fig. 4). Therefore, the values obtained in any given animal were averaged over the different conditions of the study. For the eight animals, $X_r/\Delta P_{pl}$ ranged from 0.68 to 1.24 mm/cmH$_2$O and was, on average, 0.98 ± 0.04 mm/cmH$_2$O.

For any given volume of ascites in each individual animal, the measured value of $X_r/\Delta P_{pl}$ was then multiplied by the loss in $\Delta P_{pl}$ observed during breathing with this particular volume to yield the increase in $X_r$ attributable to the pressure loss, and this increase was then added to the $X_r$ measured during breathing in the control condition to compute the $X_r$ that would be observed during ascites if the loss in $\Delta P_{pl}$ were the only operating factor. The values of $X_r$ thus predicted for all volumes of ascites in the eight animals are compared with the measured values in Fig. 5. Although the predicted values are lower than the measured values at all volumes from 100 to 200

![Fig. 2. Traces of $X_r$ of the fourth rib (cranial displacement upward), changes in pleural pressure ($P_{pl}$) and $P_{ab}$, and parasternal and external intercostal EMG activity (integrated signals) obtained from a representative animal during resting breathing in the control condition (A) and in the presence of severe ascites (150 ml/kg; B). $X_r$ was substantially greater in the presence of ascites than during control, and $\Delta P_{pl}$ was much smaller. Parasternal intercostal inspiratory activity was also greater in ascites, whereas external intercostal activity was unchanged.](http://jap.physiology.org/)
ml/kg, the difference corresponded to only 30–35% of the observed increase in $X_r$.

**DISCUSSION**

Studies of the mechanics of the diaphragm in dogs and rabbits have clearly demonstrated that the action of the muscle on the rostral portion of the rib cage is exclusively related to the fall in $P_{pl}$ (3, 10). In the presence of ascites, however, abdominal elastance is increased (24). The descent of the diaphragm in response to a given activation, therefore, is reduced, so that the zone of apposition of the diaphragm to the rib cage is increased, and $\Delta P_{ab}$ is greater. As a result, the “appositional” force of the diaphragm should be increased (12, 28). In addition, because the diaphragm in ascites is displaced cranially at end expiration and shortens less during contraction (22, 24), its muscle fibers are longer and should exert a greater cranially oriented force at their costal insertions. Consequently, it would be expected that in ascites, the inspiratory action of the diaphragm on the lower ribs would be increased and that this action would be transmitted, at least in part, to the rostral portion of the rib cage.

In agreement with this prediction, stimulation of the phrenic nerves in the presence of pneumothorax caused little or no axial displacement of rib 4 in the control condition and produced a cranial displacement of the rib in the presence of ascites (Fig. 1). Moreover, the cranial rib displacement increased in magnitude as the volume of ascites increased, thus confirming that ascites does confer on the diaphragm an inspiratory action on the rostral portion of the rib cage. However, the degree of activation of the diaphragm during supramaximal, tetanic phrenic nerve stimulation is much larger than that during spontaneous breathing, as shown by the values of $\Delta P_{ab}$ obtained in the two experiments of the study. Whereas $\Delta P_{ab}$ during phrenic stimulation with 200 ml/kg ascites was 21 cmH$_2$O, $\Delta P_{ab}$ during spontaneous breathing with the same volume of ascites was only 3 cmH$_2$O (Fig. 3C). As the magnitude of rib displacement in the first instance was 1.2 mm, a reasonable estimate for the cranial rib motion in the second instance would therefore be 1.2/7, i.e., ~0.2 mm. On the other hand, relative to the control condition, the cranial rib motion during spontaneous breathing with 200 ml/kg ascites increased, on average, by 4 mm (Fig. 3A). The conclusion can therefore be drawn that the action of the diaphragm on the rib cage plays only a minor role in causing the increased inspiratory rib elevation in ascites. Consequently, the bulk of this increase
must be related either to the decrease in ΔP_pl, or to the increase in the force exerted by the inspiratory intercostals on the ribs, or to a combination of both factors.

To quantify the contribution of the loss in ΔP_pl and separate this contribution from that of the increase in intercostal muscle force, we multiplied for each individual animal the pressure loss by the ratio of X_r over ΔP_pl obtained during passive inflation. Indeed, this ratio reflects the gain with which a 1-cmH2O rise in P_pl during passive inflation displaces the ribs cranially or, alternatively, the gain with which a 1-cmH2O fall in P_pl during inspiration opposes the cranial rib displacement produced by the action of the inspiratory intercostal muscles. The value thus measured for X_r/ΔP_pl in our animals was similar to that found previously (10) and averaged 0.98 mm/cmH2O and, when this value was multiplied by the loss in ΔP_pl observed in the presence of ascites, it appeared that the pressure loss accounted for about two-thirds of the increase in cranial rib displacement (Fig. 5). As a corollary, only a third of the increase in cranial rib displacement observed in ascites was related to the increase in intercostal muscle force.

In agreement with our previous study (24), all animals showed an increase in parasternal intercostal EMG activity with ascites (Fig. 3D), so that at 200 ml/kg, the peak height of the integrated EMG signal was 161% of the value recorded during control. This increase is consistent with the view that the muscles developed greater force on the ribs. However, the quantitative analysis of the results also suggests that in ascites, the inspiratory intercostals were, in fact, less effective in pulling the ribs cranially than they were in the control condition.

As previously pointed out (10), the observed (net) cranial rib displacement (X_r) that takes place during inspiration in a given condition is determined by the balance between the force applied by the inspiratory intercostals on the ribs and the force exerted by ΔP_pl. This balance can, as a first approximation, be expressed by the following equation:

\[ X_r = a(F) + b(ΔP_{pl}) \]  

(1)

where F is muscle force, a is the cranial rib displacement produced by a unit muscle force, and b is the axial rib displacement corresponding to a ΔP_pl of 1 cmH2O (i.e., 0.98 mm/cmH2O). For the control condition, considering that F equals 1 and substituting for X_r (3.5 mm) and ΔP_pl (−6.4 cmH2O) yields a = 9.74 mm. On the other hand, in the presence of 200 ml/kg ascites, parasternal intercostal EMG activity was 161% of the control value. Therefore, if the assumption is made that the force developed by the parasternal intercostals is linearly related to the amount of inspiratory activity, F in severe ascites would be 1.6, and substituting for X_r (7.5 mm) and ΔP_pl (−3.6 cmH2O) yields a = 6.89 mm. Furthermore, in the dog, coordinated contraction of the parasternal intercostals and external intercostals during spontaneous breathing, including during breathing after complete diaphragmatic paralysis, displaces the ribs cranially and outward along the same trajectory as passive inflation does (13). In other words, in the presence of 200 ml/kg ascites, the gain with which a given intercostal force pulls the ribs cranially and outward would be ~30% smaller than in the control condition.

The mechanism of the adverse effect of ascites on the intercostal effectiveness on the ribs is unclear, but it is worth pointing out that in contrast to the parasternal intercostals, activity in the external intercostals remained unchanged at 200 ml/kg ascites (Fig. 3D). With smaller volumes of ascites, external intercostal activity even tended to decrease, thus confirming that the two sets of intercostal muscles are governed by different control mechanisms (9). Thus, the parasternal intercostals are primarily, if not exclusively, governed by central mechanisms, and their response to ascites is probably the result of the increased hypercapnic drive (24). On the other hand, activity in the external intercostals of the rostral portion of the rib cage is also determined by afferent inputs from the abundant muscle spindles contained in the muscles (14) and

Fig. 4. X_r of the fourth rib corresponding to a 1-cmH2O rise in ΔP_pl during passive lung inflation in the presence of increasing ascites. Individual values were obtained from 5 animals.

Fig. 5. Comparison between mean ± SE values of X_r (●) measured in 8 animals in the presence of increasing ascites (same data as in Fig. 3A) and the values predicted on the basis of the decrease in ΔP_pl (○). The predicted values are lower than the measured values, but the decrease in ΔP_pl alone accounted for about two-thirds of the increase in X_r with 100–200 ml/kg ascites.
from mechanoreceptors in the costovertebral joints (6, 18). As a result, when the inspiratory cranial motion of the ribs is decreased by external manipulation, parasternal intercostal activity remains unaltered, but external intercostal activity shows a reflex increase (5). Conversely, external intercostal activity is reduced when the inspiratory cranial motion of the ribs is augmented (5). To the extent that rib motion was markedly increased in the presence of ascites, the speculation can therefore be offered that,afferent discharges from the muscle spindles and rib cage joints were reduced or abolished so as to offset the facilitatory effect of the increased chemical drive and maintain external intercostal activity unchanged. Additionally, nonvagal afferent pathways have been shown to alter the pattern of respiratory muscle activation during compression or distension of abdominal viscera (15, 17, 30), so the possibility that such pathways would be involved in modulating the intercostal muscle response to ascites cannot be excluded.

The observation that external intercostal activity at 200 ml/kg ascites was unchanged relative to the control condition implies that the overall force exerted by the inspiratory intercostals in ascites was less than suggested by the increase in parasternal intercostal activity. In Eq. 1, therefore, F at 200 ml/kg ascites would be <1.6, so coefficient a would be >6.89 mm. The quantitative impact of external intercostal activity on coefficient a cannot be readily estimated. However, it is well established that in the dog, the external intercostals play a much smaller role than the parasternal intercostals in elevating the ribs during resting inspiration (4), and one would expect that the difference would be even greater in a condition, such as ascites, where parasternal intercostal activity is increased and external intercostal activity is unaltered. It is likely, therefore, that the computed decrease in intercostal effectiveness in ascites is primarily related to the parasternal intercostals themselves, rather than the external intercostals.

Because the ribs move through a rotation around the long axis of their neck, the inspiratory moment exerted on a particular rib by a given parasternal force is directly proportional to the perpendicular distance between the axis of rib rotation and the point of attachment of the muscle to the rib (33). Ascites causes a cranial displacement of the diaphragm at end expiration (20, 22, 24) and, with it, a fall in lung volume and a rise in P_pl. As a result, the ribs at end expiration are rotated cranially and the rib cage is expanded. To the extent that the axis of rib rotation is oriented dorsally, laterally, and caudally, the possibility should therefore be considered that with an expanded rib cage, the distance between the point of attachment of the parasternal intercostals on the ribs and the axes of rib rotation is smaller than in the control condition, i.e., the moment exerted by the muscles on the ribs would be smaller.

To test this possibility, we examined the measurements of rib motion and ΔP_pl obtained in a previous study (23) of the effect of lung inflation on the canine parasternal intercostals. The animals in that study had the phrenic nerves sectioned and the external intercostal muscles in all interspaces excised, so that the parasternal intercostals were the only muscles active during inspiration, and they performed spontaneous inspiratory efforts against an occluded airway at different lung volumes. Although parasternal EMG activity was constant, ΔP_pl decreased markedly as lung volume before inspiration increased, thus confirming that inflation adversely affects the pressure-generating ability of the muscles (29). However, whereas this pressure loss should have caused an increase in X_p, X_p remained unchanged as lung volume increased from functional residual capacity (FRC) to 10 cmH2O transrespiratory pressure, and it even decreased as lung volume increased further to 20 cmH2O (23). This lack of increase in X_p suggests that factors other than ΔP_pl and parasternal force operated to reduce X_p at high lung volumes, and, indeed, if one substitutes in Eq. 1 the values of X_p and ΔP_pl obtained at the different lung volumes (see Figs. 2 and 3 in Ref. 23), it appears that coefficient a was 25% lower at 10 cmH2O than at FRC and 44% lower at 20 cmH2O than at FRC. These results fully support the idea that the parasternal intercostals are less effective in pulling the ribs cranially when the rib cage is expanded, as in ascites.

In conclusion, the present observations confirmed that the inspiratory elevation of the ribs increases progressively with increasing ascites. More importantly, they demonstrated that the action of the diaphragm on the rib cage plays only a small role in determining this response. Instead, the increased rib elevation is related partly to the increased activation of the parasternal intercostals and mostly to the decrease in inspiratory ΔP_pl. The increased activation of the parasternal intercostals, in fact, translates only into an increase in rib elevation because the rib cage expansion induced by ascites makes these muscles less effective in pulling the ribs cranially.

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