Esophageal pressures in acute lung injury: do they represent artifact or useful information about transpulmonary pressure, chest wall mechanics, and lung stress?

Stephen H. Loring,1,5 Carl R. O’Donnell,2,5 Negin Behazin,1,5 Atul Malhotra,3,5 Todd Sarge,1,5 Ray Ritz,1 Victor Novack,4 and Daniel Talmor1,5

1Department of Anesthesia, Critical Care, and Pain Medicine and 2Division of Pulmonary, Critical Care, and Sleep Medicine, Beth Israel Deaconess Medical Center, 3Divisions of Pulmonary and Critical Care and Sleep Medicine, Brigham and Women’s Hospital, 4Harvard Clinical Research Institute, and 5Harvard Medical School, Boston, Massachusetts

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Loring SH, O’Donnell CR, Behazin N, Malhotra A, Sarge T, Ritz R, Novack V, Talmor D. Esophageal pressures in acute lung injury: do they represent artifact or useful information about transpulmonary pressure, chest wall mechanics, and lung stress? J Appl Physiol 108: 515–522, 2010. First published December 17, 2009; doi:10.1152/japplphysiol.00835.2009.—Acute lung injury can be worsened by inappropriate mechanical ventilation, and numerous experimental studies suggest that ventilator-induced lung injury is increased by excessive lung inflation at end inspiration or inadequate lung inflation at end expiration. Lung inflation depends not only on airway pressures from the ventilator but, also, pleural pressure within the chest wall. Although esophageal pressure (Pes) measurements are often used to estimate pleural pressures in healthy subjects and patients, they are widely mistrusted and rarely used in critical illness. To assess the credibility of Pes as an estimate of pleural pressure in critically ill patients, we compared Pes measurements in 48 patients with acute lung injury with simultaneously measured gastric and bladder pressures (Pga and Pblad). End-expiratory Pes, Pga, and Pblad were high and varied widely among patients, averaging 18.6 ± 4.7, 18.4 ± 5.6, and 19.3 ± 7.8 cmH2O, respectively (mean ± SD). End-expiratory Pes was correlated with Pga (P = 0.0004) and Pblad (P = 0.0104) and unrelated to chest wall compliance. Pes-Pga differences were consistent with expected gravitational pressure gradients and transdiaphragmatic pressures. Transpulmonary pressure (airway pressure – Pes) was −2.8 ± 4.9 cmH2O at end exhalation and 8.3 ± 6.2 cmH2O at end inflation, values consistent with effects of mediastinal weight, gravitational gradients in pleural pressure, and airway closure at end exhalation. Lung parenchymal stress measured directly as end-inspiratory transpulmonary pressure was much less than stress inferred from the plateau airway pressures and lung and chest wall compliances. We suggest that Pes can be used to estimate transpulmonary pressures that are consistent with known physiology and can provide meaningful information, otherwise unavailable, in critically ill patients.

respiratory mechanics; esophageal balloon; mechanical ventilation; positive end-expiratory pressure; plateau pressure

ACUTE LUNG INJURY (ALI) and acute respiratory distress syndrome (ARDS) are debilitating respiratory conditions that can be worsened by inappropriate airway pressures applied during mechanical ventilation (6). The ARDSNet Consortium demonstrated that mortality could be improved by reducing tidal volume (VT) and by limiting the end-inspiratory plateau pressure (Pplat) to 30 cmH2O, thereby limiting the peak stress applied to the respiratory system and lung (1). Numerous experimental studies have shown that lung injury can also be reduced by maintaining sufficient positive end-expiratory pressure (PEEP) to prevent lung collapse at end expiration (8, 9, 11, 15, 22, 23, 26, 37–39, 49). Lung inflation depends on transpulmonary pressure (airway pressure – pleural pressure), which in turn depends on characteristics of the chest wall, as well as the lung. Unfortunately, pressures within the chest cavity are rarely measured in critical illness, and, as a result, ventilator pressures are rarely adjusted to account for the pressures outside the lung. In a recent clinical trial (45), we tested a strategy of measuring esophageal pressure (Pes) to estimate transpulmonary pressure and set the PEEP applied by the ventilator. This strategy was associated with significant improvements in lung function and a trend toward improved survival, suggesting that PEEP and end-expiratory transpulmonary pressure are important determinants of lung health in this population.

Pes has been used for decades to estimate an effective pleural pressure (Ppl) between the lung and chest wall in healthy subjects and patients who are upright (10, 20, 40, 43). Because pleural pressure varies from place to place because of the gravitational gradient and other factors (27), there is no single value of pleural pressure. However, there is always an “effective” value of pleural pressure that, if it were applied to the whole pleural surface, would result in the observed lung volume and flow. To distinguish local and effective pressures, in this report, Ppl will denote the theoretical, unmeasured, effective pleural pressure that probably approximates the local pleural pressure (Ppl) as a theoretical pressure difference between the airway opening and the pleural space (34). Pt. is to be distinguished from the corresponding estimated transpulmonary pressure, usually measured with an esophageal balloon (Pt.es = airway pressure – Pes).

Despite its longstanding use in upright patients and healthy subjects, there is widespread skepticism that Pes measurements reflect Ppl in patients who are supine, especially those with critical illness (12, 21). In particular, Pes values measured in supine critically ill patients are often much greater than what many assume to be likely pleural pressures. In this report, we argue, to the contrary, that Pes can be used to estimate credible values of Ppl. To be sure, there are differences between Pes and the effective Ppl in the supine position caused by the weight of mediastinal contents and other factors. The possibility remains, however, that the inaccuracies in estimating Ppl are minor.
Physiological Measurements

Airflow was measured with a pneumotachograph (Fleisch no. 1, available from PhippsBird.com) and integrated to obtain tidal volume (VT). Airway pressure was measured at the endotracheal tube. Gastric and esophageal pressures (Pga and Pes) were measured with an esophageal balloon-catheter (Ackrad Laboratories, available from CooperSurgical.com). The balloon (9.5 cm long, 2 cm perimeter) was filled with 0.5–1.0 ml of air. Frequency response of the system was adequate (without significant delays) up to 15 Hz. Pressure, volume, and flow measurements were displayed and recorded using a custom-written program and analyzed with Windaq software (Dataq.com).

Protocol

Patients were studied in the supine position, with the head of the bed elevated 30° (to prevent ventilator-associated pneumonia), on controlled mechanical ventilation with preintervention ventilator settings. They were sufficiently sedated to permit measurements of passive elastic recoil pressures of the respiratory system during mechanical ventilation. Bladder pressure (Pblad) was measured in 36 subjects via urinary catheter using standard techniques, with 50 ml of saline in the bladder and with the transducer referenced to the level of the pubic symphysis (32). In 35 subjects in whom it was possible, the esophageal balloon-catheter was first passed through the lower esophageal sphincter into the stomach for measurement of Pga at end expiration during mechanical ventilation. In all subjects, the balloon’s tip was repositioned to 40 cm from the incisors for recording Pes using techniques validated previously (46). Balloon position in the lower esophagus, which could not be confirmed by the occlusion technique in patients who were not making respiratory efforts, was confirmed by the presence of cardiac pulsation in the pressure trace, by appropriate pressure deflections during mechanical ventilation and a gentle push on the abdomen, and, in one case, by chest X-ray. In subjects in whom the pressure was initially recorded in the stomach, a change in pressure and respiratory and cardiac waveforms during withdrawal confirmed movement of the balloon into the esophagus. Airway pressure, Pes, and Ptaes were measured during an end-inspiratory occlusion (EIO) to obtain Pplat, PeSEE, and Ptaes, respectively. The corresponding pressures during an end-expiratory occlusion (EEO) yielded total PEEP (PEEPr), PeSEE, and Ptaes. Lung elastance (El) was calculated as (Ptaes − PeSEE)/VT, and chest wall elastance (Ecw) was calculated as (PeSEE − Pes)/VT.

Statistical Analysis

Data are presented as means ± SD. Linear regression with the coefficient of determination and ANOVA (JMP, SAS Institute) were used as appropriate. Significance was assumed for P < 0.05.

RESULTS AND DISCUSSION

The subjects were seriously ill (45), and most were ventilated with a low VT and high PEEP, consistent with current recommendations (1). Table 1 shows subject characteristics, blood gas values, and preintervention ventilator settings.

Esophageal Pressure

Pes values were quite high and variable among patients. Whereas pleural pressure inferred from Pes in upright subjects is usually subatmospheric at end exhalation, PeSEE in our patients averaged 18.6 ± 4.7 cmH2O, and PeSEE averaged 22.3 ± 5.0 cmH2O. These PeSEE values are higher than those...
of 10 healthy supine subjects at relaxed functional residual
capacity (3.3 ± 3.2 cm H2O) (47). They are also higher than the
average 8.0 ± 3.1 cm H2O in 10 supine subjects of normal
weight without lung disease studied under anesthesia and
paralysis during ventilation without PEEP (2a). Several argu-
ments suggest that these high values in patients are consistent
with known pathophysiology. First, in the supine posture, Pes
is known to overestimate Ppl at midlung height by
5 cm H2O, presumably, because of the weight of mediastinal contents (17,
25, 33, 36, 47). Therefore, the effective pleural pressure is
estimated to be ~5 cm H2O lower than Pes. Second, abdominal
pressure inferred from bladder pressure is variable and greater
than normal in many critically ill patients (31, 32), suggesting
that Ppl and Pes might also be greater than normal. If the high
Pes values we measured reflect real elevations in intrathoracic
and pleural pressures, we would expect them to be associated
with commensurately high values of Pga and Pblad, which are
not subject to the effects of mediastinal weight and inhomoge-
neous lung mechanics, which are thought to affect Pes in
patients. This was, in fact, the case. The average value of
end-expiratory Pga was 18.4 ± 5.6 cm H2O, which is greater
than the average 5.6 ± 3.8 cm H2O measured in six nonobese
patients without lung disease who were anesthetized and ven-
tilated without PEEP before elective surgery (2a). Pblad averaged
19.3 ± 7.8 cm H2O, which is greater than the normal range (~12–15 cm H2O) in subjects in the supine position,
with the head of the bed elevated 30° (13). Furthermore, Pga
and Pblad were positively correlated with PseSEO (R² = 0.32,
P = 0.0004 and R² = 0.18, P = 0.0104, respectively; Fig. 1), so those patients with higher PseSEO tended to have
higher Pga and Pblad. The similar magnitude and correlation
of PseSEO with Pga and Pblad support the hypothesis that all
these measurements reflect a common, variable elevation of
pressure within the coelomic cavity in many critically ill
patients.

The difference between PseSEO and Pga in individuals (Pga −
Pes) ranged from −9.8 to 8.0 cm H2O and averaged −1.3 ± 4.8
cm H2O (Fig. 2). The Pga-PseSEO difference is changed in
opposite directions by gravitational pressure gradients (13) and
transdiaphragmatic pressure. Because the lower esophagus is
dorsal to the gastric air bubble, we would expect Pes to be
higher than Pga in supine subjects because of the gravitational
pressure gradient in the intervening tissues (including that due
to the weight of mediastinal contents noted above). On the
other hand, passive tension in the diaphragm causes a trans-
diaphragmatic pressure. We would expect that, in patients with
high abdominal pressure, the diaphragm would be stretched,
increasing its passive tension and increasing the Pga-PseSEO
difference. This expectation is borne out by the positive cor-
relation of the Pga-PseSEO difference with Pga, higher Pga values
being associated with higher Pga-PseSEO difference (R² = 0.32, P =
Transpulmonary pressure (PL), which is shown below scans.

PEEPT, which averaged 15.7 cmH2O, was much less than the simultaneously measured airway pressure (i.e., total positive end-expiratory pressure [PEEPT]). PL,esEEO is usually substantially less than PEEPT. Solid line, line of regression.

0.0004; Fig. 2), although mathematical coupling of independent and dependent variables could also explain this result. Other causes of interindividual differences between Pga and Pes include local shear-induced pressure gradients that accompany the deformation of shape-stable viscera (29), variations in gastric and esophageal muscle tone, and gravitational pressure differences associated with differences in body position (5). We suggest that Pga and Pes differ by amounts consistent with variations due to gravitational pressure gradients, deformation of solid tissues, mediastinal weight, and passive diaphragmatic tension; the latter dominates when Pga is high.

Transpulmonary Pressures at End-Expiratory Occlusion

Because PesEEO values were high, the end-expiratory PL,esEEO values tended to be low, averaging −2.8 ± 4.9 cmH2O, and PL,esEEO was less than zero in most patients (Fig. 3). PL,esEEO was much less than the simultaneously measured airway pressure (i.e., PEEPT), which averaged 15.7 ± 4.2 cmH2O.

How could PL,esEEO reasonably be negative in these patients? Some mechanisms that could affect the relations between PL, PL,esEEO, and PEEPT are depicted in Fig. 4A. First, because Pes is increased in the supine posture by the weight of mediastinal contents (see above), Pes overestimates Ppl at midlung height, and PL,esEEO underestimates Pt by ~5 cmH2O. Second, the gravitational gradient in pleural pressure, which would be more important with edematous lungs, could permit the upper (nondependent) lung regions to have a locally positive transpulmonary pressure.

Pt is defined as the pressure difference from airway to pleural space, so a negative Pt implies that pleural pressure is greater than airway pressure. Note that a negative Pt does not imply that the elastic recoil pressure of the lung (alveolar pressure − pleural pressure) is negative; recoil pressure is likely to be positive, even at low lung volume (24). Instead, a negative Pt implies that airway closure and/or alveolar flooding have prevented alveolar pressure from equilibrating with airway pressure, and alveolar pressure becomes equal to the local pleural pressure. Airway closure is a normal occurrence in older people at low lung volumes (2, 3), and static negative transpulmonary pressures at very low volumes have been demonstrated in healthy breath-hold divers who have employed glossopharyngeal exsufflation to empty their lungs below residual volume (28). Airway closure probably occurs in all lungs (of terrestrial mammals) that are held at substantially below residual volume (24). Instead, a highly negative pressure at the trachea (Thus statically negative values of Pt are likely when pressures in the thorax and abdomen are pathologically elevated.

PL,esEEO, the difference between PEEP and PesEEO, is a measure of the pressure distending the lung at end expiration and is controlled clinically by adjustment of PEEP. In our patients, PL,esEEO was negatively correlated with PesEEO (R² = 0.39, P < 0.0001) and positively correlated with PEEPT (R² = 0.21, P = 0.0011; Fig. 3), suggesting that the most important determinant of the interindividual differences in PL,esEEO (and, presumably, also end-expiratory lung volume) was PesEEO.
which depends on the chest wall, not the PEEP applied by the ventilator.

Transpulmonary Pressure at End-Inspiratory Occlusion (Plateau)

As with $P_{\text{L,esEEO}}$, $P_{\text{L,esEEO}}$ values were low, averaging $8.3 \pm 6.2$ cmH$_2$O and ranging from $-5.8$ to 26.6 cmH$_2$O. These values are much lower than the simultaneously measured airway pressures ($P_{\text{plat}}$), which averaged 30.5 $\pm$ 6.2 cmH$_2$O. How could $P_{\text{L,esEEO}}$ be so low (sometimes less than zero) at end inflation in a critically ill subject? Possible mechanisms are depicted in Fig. 4B. The weight of mediastinal contents lowers $P_{\text{L,esEEO}}$ relative to $P_L$, so $P_{\text{L,esEEO}}$ could be approximately $-5$ cmH$_2$O without implying a negative effective $P_L$. However, even after we accounted for effects of mediastinal weight, many of our estimated static transpulmonary pressures at midlung height ($P_L$) are still negative. How could end-inspiratory $P_L$ be negative? The gravitational gradient in pleural pressure could permit the upper lung regions to have a locally positive transpulmonary pressure, while the “effective” $P_L$ at midlung height remained slightly negative. Furthermore, transpulmonary pressure would be higher during inspiratory flow than during the end-inspiratory occlusion, permitting ventilation, even if $P_{\text{L,esEEO}}$ was negative. These arguments suggest that the range of $P_{\text{L,esEEO}}$ values in our subjects (after correction for mediastinal weight) could reflect similar values of $P_L$.

$P_{\text{L,esEEO}}$ values were not only positively correlated with $P_{\text{plat}}$ ($R^2 = 0.45$, $P < 0.0001$; Fig. 5) but, also, negatively correlated with $P_{\text{EsEEO}}$ ($R^2 = 0.18$, $P = 0.0026$). Thus, although end-inspiratory transpulmonary pressure is largely determined by airway pressure, it is also importantly influenced by the pressure across the chest wall and cannot be adequately predicted from $P_{\text{plat}}$ alone.

Chest Wall Elastance

Ecw was, on average, slightly greater than normal, 8.7 $\pm$ 4.7 cmH$_2$O/l, but it ranged widely from 1.3 to 21.8 cmH$_2$O/l. Perhaps surprisingly, Ecw was not correlated with $P_{\text{EsEEO}}$, implying that the slope of the pressure-volume curve of the chest wall was not correlated with the position of the curve relative to the pressure axis. Therefore, high levels of Pes at end-expiration are not, in general, associated with high Ecw. Conversely, high Ecw values are not, in general, associated with particularly high levels of $P_{\text{EsEEO}}$. Ecw was also not correlated with $P_{\text{plat}}$ or $P_{\text{L,esEEO}}$.

Implications of the Findings for Ventilator Management in ALI/ARDS

The findings presented above constitute a dilemma. If we maintain that the high Pes values measured in our subjects are artifactual (12, 21), we run the risk of ignoring important information that could be clinically useful (4). In particular, the well-documented elevations in abdominal pressure in some patients with critical illness suggest that there might be similar elevations in pleural pressure that would affect the lungs. Alternatively, if we accept the measured values of Pes and $P_{\text{L,es}}$ as meaningful, if somewhat flawed, estimates of Ppl and Pt (after a correction of $\sim 5$ cmH$_2$O), we can use these estimates to assess respiratory mechanics in ARDS/ALI. Below, we consider implications of our findings for management of mechanical ventilation.

Setting PEEP to set end-expiratory lung volume. Maintaining inflation of the lungs at end expiration is critical for oxygenation and minimization of atelectrauma (44). Usually, lung inflation at end expiration is adjusted by setting PEEP with the ventilator. However, we found that $P_{\text{L,esEEO}}$, which depends largely on the pressure across the chest wall, was variable and often substantially lower than the simultaneously measured airway pressure (PEEP$_Y$). It follows that measurement of the pressure across the chest wall ($P_{\text{EsEEO}}$) and calculation of $P_{\text{L,esEEO}}$ can help in the choice of an appropriate PEEP in such patients. This strategy was used in our earlier clinical trial (45).

The finding that pleural pressures vary widely among patients implies that the risks and benefits of applied PEEP are likely to vary from patient to patient. A given high level of PEEP in an individual with a high pleural pressure could improve oxygenation and protect the lung from repetitive alveolar collapse, whereas the same level of PEEP in an individual with low pleural pressure could expose the lung to injurious stress at end inspiration. This may account for the difficulty of determining an optimal level of applied PEEP in clinical trials (18). Effects of PEEP on the lungs cannot be fully appreciated without consideration of the effects of the chest wall on transpulmonary pressure.

Ecw and Pes. The chest wall in ARDS has been described as sometimes having low compliance (19). High intrathoracic pressures and low chest wall compliance can be caused by abdominal distension (42). However, high pressures and low compliance need not occur together. Note that elastance, the inverse of compliance, is the change in pressure for a given change in volume and does not predict the pressure at any volume. Our finding that Ecw was not universally elevated is consistent with previous findings in 70 patients with acute respiratory failure (46) and challenges a common perception that high Pes values are due to low chest wall compliance. The state of inflation of the lung depends more on the value of Pes than on the increase in Pes during tidal inflation (elastance). Therefore, the lack of correlation between $P_{\text{EsEEO}}$ and Ecw underscores the importance of measuring the resting values of

![Fig. 5. Estimated transpulmonary pressure at end-inspiratory occlusion ($P_{\text{L,esEEO}}$) vs. simultaneously measured airway pressure ($P_{\text{plat}}$). $P_{\text{L,esEEO}}$ is substantially less than $P_{\text{plat}}$. Solid line, line of regression.](image-url)
Pes, not merely the tidal excursions in Pes used to calculate Ecw.

**Lung stress in ALI/ARDS and the effects of the chest wall.**

The end-inspiratory airway pressure, \( P_{\text{plat}} \), is often used as an index of lung stress during mechanical ventilation and as a means to assess lung injury in ALI/ARDS (1). Checkley et al. (6) recently analyzed preenrollment ventilation parameters in 2,451 patients with ALI/ARDS entered into several of the ARDSnet Trials. They showed that higher preenrollment \( P_{\text{plat}} \) values strongly predicted mortality and reasoned that the reciprocal relationship between \( P_{\text{plat}} \) and respiratory system compliance suggests that high \( P_{\text{plat}} \) and low compliance provide similar information, both indicating lung injury (16). Thus, for a given \( V_T \), less compliant lungs would result in a greater increase in airway pressure and higher \( P_{\text{plat}} \).

With Pes measurements, it is theoretically possible to measure end-inspiratory lung stress directly. When airways are open and the central airways communicate with alveoli, \( P_{\text{EESO}} \) is an estimate of the average end-inspiratory stress of the lung parenchyma (i.e., the elastic recoil pressure of the lung) (34).

In a recent report, Chiumello et al. (7) analyzed the stress applied to the lungs of patients with ALI/ARDS and patients with normal lungs by estimating transpulmonary pressure with an esophageal balloon. However, they equated the end-inspiratory stress applied to the lung with the tidal increase in transpulmonary pressure from that at relaxation volume, discounting the initial (baseline) pressure by subtraction. This approach is common in studies of critically ill patients (14, 19, 30, 35, 41, 42, 48). However, we reasoned that the prestress before inflation might be quantitatively important. For example, the end-inspiratory parenchymal stress after a tidal inflation from a low initial stress (e.g., after inflation from a low lung volume) would be less than that after inflation from a high initial stress (after inflation from a high lung volume), even though the changes in stress might be identical. Similarly, if the lungs were being compressed by a high \( P_{\text{P}} \) at end expiration, the transpulmonary pressure could increase substantially to initiate inflation without causing high end-inspiratory pressures or stress.

With this in mind, we evaluated the possible contribution of prestress to end-inspiratory lung stress in our patients. Parenchymal stress at end inflation can be assessed by measuring the transpulmonary pressure, \( P_{\text{L,EESO}} = P_{\text{L,SEEEO}} + \Delta P_{\text{L}} \), in any individual the parenchymal stress would be increased by raising \( P_{\text{L,SEEEO}} \), \( E_L \), or \( V_T \). We sought to determine how interindividual differences in postinflation \( P_{\text{L,SEEEO}} \) depend on differences in each of these variables among our subjects. \( P_{\text{L,SEEEO}} \) values were correlated with \( P_{\text{L,SEEEO}} \) (\( R^2 = 0.62 \), \( P < 0.0001 \); Fig. 6A), correlated with \( E_L \) (\( R^2 = 0.23 \), \( P = 0.0006 \); Fig. 6B), and not correlated with \( V_T \) (Fig. 6C). Therefore, in our cohort, lung parenchymal stress at end inflation was most importantly determined by \( P_{\text{L,SEEEO}} \), the prestress before inflation. \( P_{\text{L,SEEEO}} \) was not evaluated by Chiumello et al. (7) because of concerns about artifacts in PesEEO, but this practice ignores the influence of pressure inside the chest wall, which could be important.

To assess the contribution of prestress to the estimation of end-inspiratory parenchymal stress, we compared directly measured values of end-inspiratory transpulmonary pressure in our subjects with values calculated using the equation of Chiumello et al. (7): \( \Delta P_{\text{L(stress)}} = \Delta P_{\text{aw}} \times \frac{E_L}{E_L + \text{Ecw}} \), where \( \Delta P_{\text{aw}} \) is the tidal increase in airway pressure (i.e., \( P_{\text{plat}} - \text{PEEP}_T \)). The end-inspiratory lung stress calculated by this
equation, which does not account for prestress, averages 22.9 ± 6.5 cmH₂O and ranges from 7.4 to 38.7 cmH₂O, which is much higher than the directly measured P_teso, which averaged 8.3 ± 6.2 cmH₂O and ranged from −5.8 to 26.6 cmH₂O (Fig. 7). Even if we assume that Pes is 5 cmH₂O higher than pleural pressure measured at midlung height, as in our earlier clinical trial (45), the two estimates of lung stress differ by 9.6 ± 5.0 cmH₂O. Theoretically, the directly measured end-inspiratory transpulmonary pressure (P_teso) is a measure of end-inspiratory lung parenchymal stress, whereas ΔP_t(stress) of Chiumello et al. is a measure of the increase in stress from relaxation volume, which depends only on EL and inflation volume. Thus, ΔP_t(stress) provides an incomplete measure of the effects of the chest wall on lung stress.

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DISCLOSURES

No conflicts of interest are declared by the author(s).

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