Published in final edited form as:
Crit Care Med. 2006 May ; 34(5): 1389–1394.

Esophageal and transpulmonary pressures in acute respiratory failure*

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Abstract

Objective—Pressure inflating the lung during mechanical ventilation is the difference between pressure applied at the airway opening (P_{ao}) and pleural pressure (P_{pl}). Depending on the chest wall's contribution to respiratory mechanics, a given positive end-expiratory and/or end-inspiratory plateau pressure may be appropriate for one patient but inadequate or potentially injurious for another. Thus, failure to account for chest wall mechanics may affect results in clinical trials of mechanical ventilation strategies in acute respiratory distress syndrome. By measuring esophageal pressure (P_{es}), we sought to characterize influence of the chest wall on P_{pl} and transpulmonary pressure (P_L) in patients with acute respiratory failure.

Design—Prospective observational study.

Setting—Medical and surgical intensive care units at Beth Israel Deaconess Medical Center.

Patients—Seventy patients with acute respiratory failure. *Interventions:* Placement of esophageal balloon-catheters.

Measurements and Main Results—Airway, esophageal, and gastric pressures recorded at end-exhalation and end-inflation P_{es} averaged 17.5 ± 5.7 cm H_2O at end-expiration and 21.2 ± 7.7 cm H_2O at end-inflation and were not significantly correlated with body mass index or chest wall elastance. Estimated P_L was 1.5 ± 6.3 cm H_2O at end-expiration, 21.4 ± 9.3 cm H_2O at end-inflation, and 18.4 ± 10.2 cm H_2O (n = 40) during an end-inspiratory hold (plateau). Although P_L at end-expiration was significantly correlated with positive end-expiratory pressure ($p < .0001$), only 24% of the variance in P_L was explained by P_{ao} ($R^2 = .243$), and 52% was due to variation in P_{es}.

Conclusions—In patients in acute respiratory failure, elevated esophageal pressures suggest that chest wall mechanical properties often contribute substantially and unpredictably to total respiratory impedance, and therefore P_{ao} may not adequately predict P_L or lung distention. Systematic use of esophageal manometry has the potential to improve ventilator management in acute respiratory failure by providing more direct assessment of lung distending pressure.

Keywords

lung injury; pleural pressure; ventilator; positive end-expiratory pressure; acute respiratory distress syndrome

*See also pp. 1554 and 1556.

The authors have no financial interests to disclose.

Acute respiratory distress syndrome (ARDS) remains a disease of high mortality rate despite recent therapeutic advances (1). Although mechanical ventilation can be lifesaving for afflicted individuals, inappropriate use of the ventilator can itself promote lung injury. Ventilator-associated lung injury has a variety of causal mechanisms demonstrated in animal models including cyclic overdistension and collapse. Overdistension injury is the result of excessive stress at end-inflation, presumably due to high transpulmonary pressure, whereas "atelectrauma" is injury induced by repetitive closing of alveolar units (2–4), and may reflect insufficient transpulmonary pressure at end-exhalation. Although overdistension may be avoided by use of low tidal volumes, which limit end-inspiratory pressure (5), atelectrauma may be limited by the application of sufficient levels of positive end-expiratory pressure (PEEP).

Ventilator-induced damage to the lungs arguably depends on the transpulmonary pressure (P_L), which is pressure at the airway opening (P_{ao}) minus pleural pressure (P_{pl}), whereas current recommendations for management of ARDS specify limits for pressure applied across the whole respiratory system, $P_{ao} - P_{bs}$, where P_{bs} is pressure at the body surface. This approach could be seriously misleading if P_{pl} were to vary substantially among patients. In healthy subjects and upright spontaneously breathing patients, P_{pl} is often estimated by measuring esophageal pressure (P_{es}); however, this is rarely done in patients with acute injury, possibly because of a widespread, but largely untested, belief that artifacts make P_{es} useless as an estimate of P_{pl}. In this report, we describe the variation in P_{es} across a cohort of patients with ARF. In our interpretation of these data we make the explicit assumption that P_{es}, corrected for a positional artifact, reflects an effective P_{pl} in critically ill patients as it does in healthy individuals. Further clinical investigation is needed to confirm or disprove this assumption.

Uncharacterized variations in P_{pl} may have contributed to inconsistent outcomes among clinical trials of ventilation strategies in ARDS. For example, whereas one large-scale randomized trial demonstrated a survival benefit from use of low tidal volume ventilation, results from other studies have been equivocal (5–7). It is possible that in some patients with high P_{pl}, low tidal volume ventilation coupled with inadequate levels of PEEP results in cyclic alveolar collapse at end-expiration. In such cases, resulting at-electrauma might negate the benefit of limiting tidal volume. Similarly, higher levels of PEEP have been shown to be lung-protective in numerous animal models of ARDS (8) but have demonstrated inconsistent benefit in clinical investigations (2,9). This too may reflect failure to account for P_{pl}, leading to under- or overapplication of PEEP in some patients as well as misinterpretation of high plateau airway pressures as evidence of lung overdistension (10,11). We suggest that by measuring P_{es} to estimate transpulmonary pressure, mechanical ventilator settings could be more appropriately customized to accommodate interindividual variations in lung and chest wall mechanical characteristics. Such an individual approach may reduce the risk for further lung injury in patients with ARDS undergoing mechanical ventilation (10,12,13).

In this study, we measured P_{es} to estimate pleural pressure in ventilated patients with or at risk for acute lung injury. We sought to determine the relationship between measured P_{ao} and the associated transpulmonary pressures at both end-exhalation and end-inflation. We reason that such measurements may identify physiologic variables important in minimizing overdistension injury and atelectrauma in mechanically ventilated patients.

METHODS

Patients

We studied 70 patients with acute respiratory failure, 12% of the patients with this diagnosis admitted to the medical and surgical intensive care units at Beth Israel Deaconess Medical Center in 2002–2003. The decision to perform esophageal manometry was clinical, based on

actual or anticipated difficulty with mechanical ventilation, and there were no systematic selection criteria. Our institutional review board approved this observational study through review of medical records.

Measurements

Patients were supine with the bed at 0–30° head up. Air flow was measured with a pneumotachograph (Fleisch No. 1). Gastric and esophageal pressures were measured with a thin-walled vinyl balloon-catheter inflated with 0.5–1.0 mL of air (Ackrad Laboratories, Cranford, NJ). (The larger volume of air was used to prevent artifactually low readings of high esophageal pressures caused by displacement of gas from the balloon into the compliant pressure tubing and transducers.) P_{ao} was measured simultaneously. Pressure transducers were calibrated with a water manometer. Pressure and volume signals were digitized (DI 700, Dataq Instruments, Akron, OH) and flow was integrated to yield volume change using custom recording software (Npulmo, Emil Millet, Boston, MA). Volume was calibrated with a 3-L syringe. The balloon-catheter was first passed by nose or mouth into the stomach with its tip 60 cm from the incisors or nares to measure gastric pressure (P_{ga}) and then withdrawn to 40 cm to measure P_{es}. Proper balloon position was confirmed in all patients by observing an appropriate change in the pressure tracing as the balloon was withdrawn into the thorax (changes in pressure waveform, mean pressure, and cardiac oscillations). With the balloon in the esophagus, the airway was occluded at end-inspiration and end-expiration to obtain static measurements. In patients who were making respiratory efforts, correct balloon position could be confirmed retrospectively by the presence of nearly equal fluctuations in P_{ao} and P_{es} during inspiratory efforts against an occlusion (14).

Analysis

To estimate P_L, we assumed that pleural pressure at mid-lung height was 5 cm H_2O lower than measured esophageal pressure. This correction was based on measurements in ten healthy volunteers (15) showing that P_{es} in the supine position was 3 ± 2 cm H_2O greater than upright at the same lung volume and on the observation in several patients that P_{es} was 2 cm H_2O higher when the balloon air volume was increased from 0.5 to 1.0 mL. Thus, the estimated $P_L = P_{ao} - P_{es} + 5$. Elastances of the respiratory system (E_{RS}), chest wall (E_{CW}), and lung (E_L) were calculated as changes in P_{ao}, P_{es}, and P_L between end-expiratory and end-inspiratory airway occlusions (holds) divided by tidal volume. Because patients often made respiratory efforts during holds, we also calculated chest wall elastance from P_{es} at zero flow during tidal ventilation (E_{CWTV}). E_{CWVT} was highly correlated with E_{CW}, and for simplicity, we report only E_{CWVT}.

Not all data were available in all patients. In 25 patients, P_{ga} was not measured, usually because we were unable to pass the catheter past the gastroesophageal junction. Thirty-four of the patients were making spontaneous breathing efforts, and when breathing efforts coincided with the times of pressure measurements needed to calculate certain parameters, such as E_{CWVT}, these parameters were not reported for those patients. Similarly, we avoided collecting data at times of esophageal spasms, which caused slow wandering increases in the average P_{es} that usually subsided in about 20 secs. The number of observations for each parameter, if <70, is noted with the mean and $_{SD}$.

Data Analysis and Statistics

Recordings were analyzed using Windaq (Dataq Instruments, Akron, OH) and statistical software (JMP, version 5, SAS Institute, Cary, NC). We tested correlations between parameters using linear regression and differences among groups using analysis of variance or Student's *t*-test. We explored the association between ventilator parameters and mortality by contingency table with chi-square analysis. Two-tailed statistical significance was assumed for $p < .05$.

RESULTS

Our patients had characteristics typical of patients with acute respiratory failure at an academic medical center (Table 1). The overall mortality rate was 29%, consistent with values reported in the literature for mixed medical/surgical populations with ARDS (5,9). Initial ventilator settings included tidal volume 487 ± 124 mL or 7.4 ± 1.9 mL/kg ideal body weight (n = 67), frequency 24.7 ± 13.9 min^{-1}, and PEEP 14.2 ± 4.5 cm H_2O (n = 69). Tidal volume tended to be slightly lower in patients who died, perhaps as a result of more conservative ventilator management in the sicker patients, but the results did not reach significance (6.90 ± 0.45 vs. 7.56 ± 0.26 mL/kg, $p = .27$).

Esophageal balloon position was assessed retrospectively in the 20 patients who were making respiratory efforts during the end-expiratory occlusion (Fig. 1). Efforts against the occlusion produced similar changes in P_{ao} and P_{es}, indicating proper balloon position. In five patients, we tested the dependence of P_{es} on balloon air volume by inflating the esophageal balloon sequentially with 0.5 and 1.0 mL of air. The increase in P_{es} associated with the higher balloon volume was 1–3 cm H_2O, indicating a moderate sensitivity of P_{es} to balloon air volume.

P_{es} averaged 17.5 ± 5.7 cm H_2O at end-expiration and 21.2 ± 7.7 cm H_2O at end-inflation (n = 69) and was not different in passive patients and those making active respiratory efforts ($p = .64$ and .33, respectively). P_{es} at end-expiration was not significantly correlated with PEEP ($R^2 = .054$, $p = .055$, n = 69), and at end-inspiration Pes was weakly correlated with P_{ao} ($R^2 = .188$, $p = .0002$, n = 69, Fig. 2).

Estimated P_L was 1.5 ± 6.3 cm H_2O at end-expiration, 21.4 ± 9.3 cm H_2O at end-inflation, and 18.4 ± 10.2 cm H_2O (n = 40) during an end-inspiratory hold (plateau). P_L at end-expiration was, as would be expected, significantly correlated with both PEEP and P_{es}. However, only 24% of the variance in P_L was explained by P_{ao} ($R^2 = .243$, $p < .0001$, n = 69), whereas 51% was explained by P_{es} ($R^2 = .508$, $p < .0001$, n = 69, Fig. 3). As shown in Figure 3, at any given value of P_{ao}, there was a substantial range of P_L, and it was therefore not possible to accurately predict P_L from P_{ao}. Nor could P_L be predicted from tidal volume; P_L during the end-inspiratory hold was not correlated with tidal volume ($R^2 = .036$, $p = .257$, n = 38, Fig. 4).

P_L at end-expiration was not different between passive and actively breathing patients, but both P_L and P_{ao} at end-inflation were lower among patients who were actively breathing (17.8 vs. 24.9 cm H_2O, $p < .001$ for P_L, and 33.1 vs. 42.2 cm H_2O, $p < .0001$ for P_{ao}). These differences probably reflect the fact that the sicker patients, who had stiffer lungs, were more likely to be deeply sedated and/or paralyzed and thus passive (Fig. 3).

P_{es} was not correlated with obesity as assessed by body mass index at end-expiration ($R^2 = .051$, $p = .069$) or at end-inspiration ($R^2 = .032$, $p = .152$, n = 66). Similarly, chest wall stiffness, as indicated by E_{CWTV}, was not significantly correlated with body mass index ($R^2 < .001$, $p = .975$, n = 32).

P_{es} at end-expiration was not significantly correlated with stiffness of the chest wall as estimated by E_{CWTV} ($R^2 = .011$, $p = .052$, n = 35), although P_{es} was correlated with E_{CWTV} at end-inflation ($R^2 = .43$, $p < .0001$, n = 35, Fig. 5).

Gastric pressure at end-expiration (16.6 ± 6.8 cm H_2O, n = 44) was similar to esophageal pressure (17.5 ± 5.7 cm H_2O), and esophageal pressure was significantly correlated with gastric pressure ($R^2 = .354$, $p < .0001$, n = 44, Fig. 6).

DISCUSSION

Our finding that P_{es} was relatively high and unpredictable, given the assumption that P_{es} reflects pleural pressure, suggests a substantial influence of chest wall characteristics on ventilatory mechanics in acute lung injury. We found that P_{es} was on average unexpectedly high in our patients, averaging 17 cm H_2O at end-expiration and 21 cm H_2O at end-inflation, and P_{es} varied widely among patients with acute lung injury, both at end-inflation and at end-expiration (Fig. 2). High values of P_{es} could not be reliably predicted from body mass index, which is consistent with previous work suggesting that obese individuals often have a normally compliant chest wall despite high end-expiratory pleural pressures. Similarly, P_{es} could not be predicted from chest wall stiffness, and P_{es} was often quite high in patients with normal chest wall elastance. The higher P_{es} values resulted in low values of estimated P_L, and in the majority of patients, PEEP was inadequate to maintain P_L positive at end-exhalation. Similarly, P_L at the end-inspiratory plateau was often much lower than P_{ao} (Fig. 3), and P_L was not predictable from tidal volume (Fig. 4).

We found that P_{es} and P_{ga} at end-expiration are similar in magnitude and correlated. This implies that in most individuals, the transdiaphragmatic pressure was low at end-expiration, and it suggests that measurement of intra-abdominal pressure may be useful clinically where esophageal manometry is not available. Malbrain et al. (16) recently observed that intra-abdominal hypertension is common among critically ill patients. Their abdominal pressures, estimated from bladder pressure, were similar to the P_{ga} we observed at end-expiration (13.2 vs. 16.6 cm H_2O), supporting our conclusion that pressures within the abdomen and chest wall of critically ill patients are often markedly positive. In the patients with the highest P_{ga}, however, P_{ga} was much greater than P_{es}, consistent with abdominal compartment syndrome in those patients causing cephalad displacement of the diaphragm and substantial transdiaphragmatic pressure (Fig. 6).

Are Esophageal Pressures Valid?

Some authors have argued that the use of esophageal pressure as an estimate of pleural pressure is problematic in supine, mechanically ventilated patients (12,17). In the supine posture, esophageal pressure is thought to be influenced by overlying cardiac weight, thus overestimating the pressure within the pleural space at low lung volumes (14,17,18). In addition, injured lungs may exhibit increased density and nonuniform mechanical characteristics, which increase gravitational and spatial gradients in pleural pressure. On the other hand, at high lung volumes, the absolute value of esophageal pressure is thought to underestimate the actual pressure measured in the pleural space (19,20). Avoiding these possibilities, most investigators have reported only changes in esophageal pressure and transpulmonary pressure, ignoring and subtracting the baseline pressure itself (19,20). This practice ignores information that may be potentially useful.

Although there is widespread doubt that P_{es} is useful for estimating P_{pl} in supine patients, this proposition has not been tested systematically. Recently, Pelosi et al. (19) showed that P_{es} serves as a good estimate of pleural pressure measured directly at mid-lung height in animals. In ten normal patients, we assessed the contributions of mediastinal compression (cardiac weight) and lung volume change to P_{es} measured in various body postures (15) and confirmed earlier findings that the contribution of mediastinal weight is rather small (3 ± 2 cm H_2O, range 0 –7 cm H_2O) and relatively consistent. In the present study, we correct for this effect (3 cm H_2O) and the effect of esophageal balloon air volume (2 cm H_2O) by subtracting 5 cm H_2O from the estimated P_L. To the extent that other uncontrolled effects due to lung pathology cause inaccuracies that are small relative to individual variations in pleural pressure, P_{es} would be useful for estimating P_L in patients.

We found that in many patients on therapeutic ventilator settings, P_{es} was often high enough to cause estimated P_L to be negative, especially at end-expiration. We do not interpret this finding as indicating a negative elastic recoil pressure of the lung (negative transalveolar pressure). Rather, we suggest that airway closure during exhalation causes alveolar pressure in some regions to be higher than P_{ao} and P_L to be negative. Additionally, regional variations in pleural pressure may cause P_{es} (and P_{pl} at mid-lung height) to be higher than P_{pl} near the nondependent lung, allowing part of the lung to be ventilated while estimated P_L is negative.

Clinical Implications

The interpretation of our findings requires a willingness to consider that measured values of esophageal pressure reflect pleural pressure, albeit with some uncertainty due to spatial and gravitational variations in pleural and/or esophageal pressure. The decision to use P_{es} to estimate P_{pl} depends, in part, on the relative magnitudes of P_{es} and the pressures applied by the ventilator. For example, consider two of our patients who had end-inspiratory plateau (P_{ao}) pressures of 42 cm H_2O; one had a corresponding P_L of 10 cm H_2O, and the other had a corresponding P_L of 31 cm H_2O. Despite relatively high PEEP, the former patient demonstrated a negative end-expiratory P_L. We have observed many such hypoxemic patients in whom gastric and esophageal pressures were high and lung volumes and lung compliance were low. In these patients, increasing PEEP to very high levels, and achieving a positive P_L, improved apparent lung compliance and increased blood oxygenation, consistent with an important influence of the chest wall on ventilatory mechanics in acute lung injury.

The recently published results of the ALVEOLI trial demonstrated no significant benefit from moderately high levels of PEEP among patients with acute lung injury and ARDS (9), despite compelling experimental and clinical data showing that higher PEEP is protective (2,21). One possible explanation is that PEEP was applied uniformly without regard to each patient's pleural pressure. The adjustment of tidal volume and PEEP to limit each patient's estimated P_L (e.g., between 0 and 30 cm H_2O) could avoid overdistending the lungs of some patients or underventilating the lungs of others leading to hypercapnea, dyspnea, and increased requirements for sedation.

Many investigators have suggested techniques to adjust mechanical ventilator settings based on other anatomical or physiologic parameters. Quasi-static pressure-volume curves based on airway pressure have been used in this context to allow the setting of PEEP to prevent collapse at end-exhalation (below the lower inflection point) and to limit overinflation (above the upper inflection point). However, such techniques fail to distinguish the mechanical impact of the chest wall from that of the lung. Using the airway pressure time curve to calculate the "stress index" of the lung has been suggested but has not been systematically tested in humans (22, 23). Other investigators have estimated regional lung volumes using computed tomography or electrical impedance tomography to maximize lung recruitment and minimize lung injury (24). However, these techniques for estimating lung inflation are expensive, are time consuming, and require further validation before being adopted for widespread clinical use. Esophageal manometry offers an easier and potentially useful technique that deserves further study in clinical ARDS trials.

Limitations

We acknowledge the following limitations to our study. First, because patients were not enrolled in a systematic fashion, there may be a referral bias that may affect the generalizability of our findings. However, the demographic characteristics of our patients were representative of the patients in ICU at our institution, suggesting no major systematic enrollment bias. Second, because our study was observational, some of our findings may have been influenced by prior ventilator manipulations on the part of the referring clinician. Thus, we were unable

to determine whether a low tidal volume was chosen based on a measured high airway pressure, poor gas exchange, or other factors. Similarly, selection of PEEP may have been influenced by oxygenation criteria and hemodynamic factors. Third, because ours was not a prospective randomized trial, we cannot draw conclusions about the impact of our findings on clinical outcome. Such a trial is underway in our institution.

Finally, the busy clinician may ask whether esophageal manometry offers sufficient benefit to justify its use in the intensive care unit. Measurement of esophageal pressure and titration of ventilation based on these measurements take approximately 30 mins of effort by two or three investigators. Other such time- and resource-intensive early interventions, such as cardiac catheterization for acute myocardial infarction or early goal-directed therapy in sepsis, have demonstrated significant benefits. Previous studies in ARDS have demonstrated significant reductions in mortality rate by careful management of mechanical ventilation. We suggest that the additional intervention required for esophageal pressure measurement deserves further study as it may yield a clinically significant benefit.

Acknowledgements

Supported, in part, by grant HL-52586 from the National Heart Lung and Blood Institute, Bethesda, MD.

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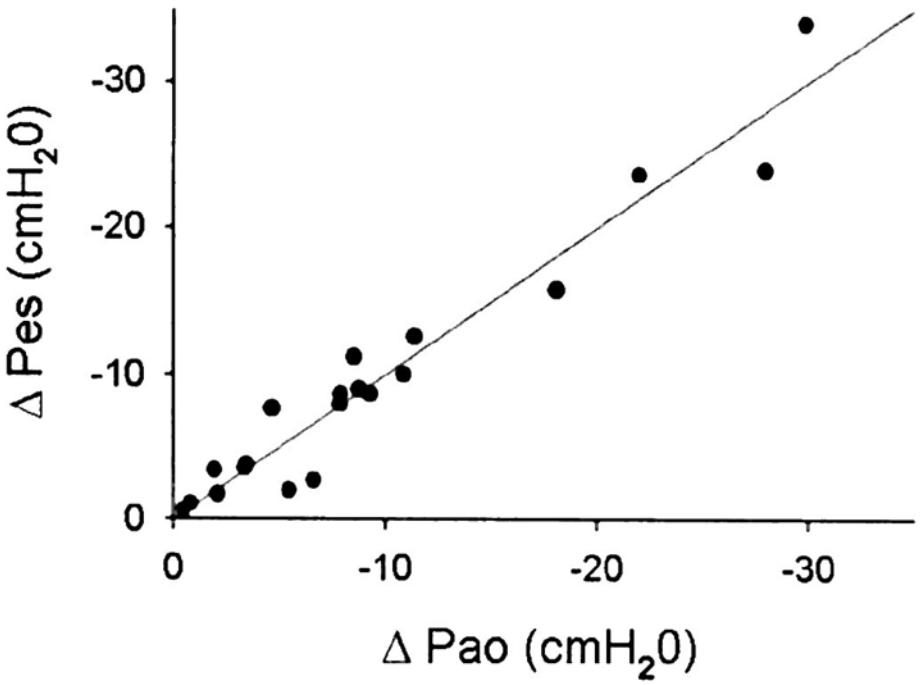

Figure 1.

Changes in airway opening pressure (ΔP_{ao}) and esophageal pressure (ΔP_{es}) during an inspiratory effort against an occluded airway at end-expiration in 20 patients who were active during the maneuvers. Line is the line of identity. Changes in P_{es} correspond closely to changes in P_{ao} ($R^2 = .937$, $p < .0001$), suggesting that the esophageal balloon is correctly positioned.

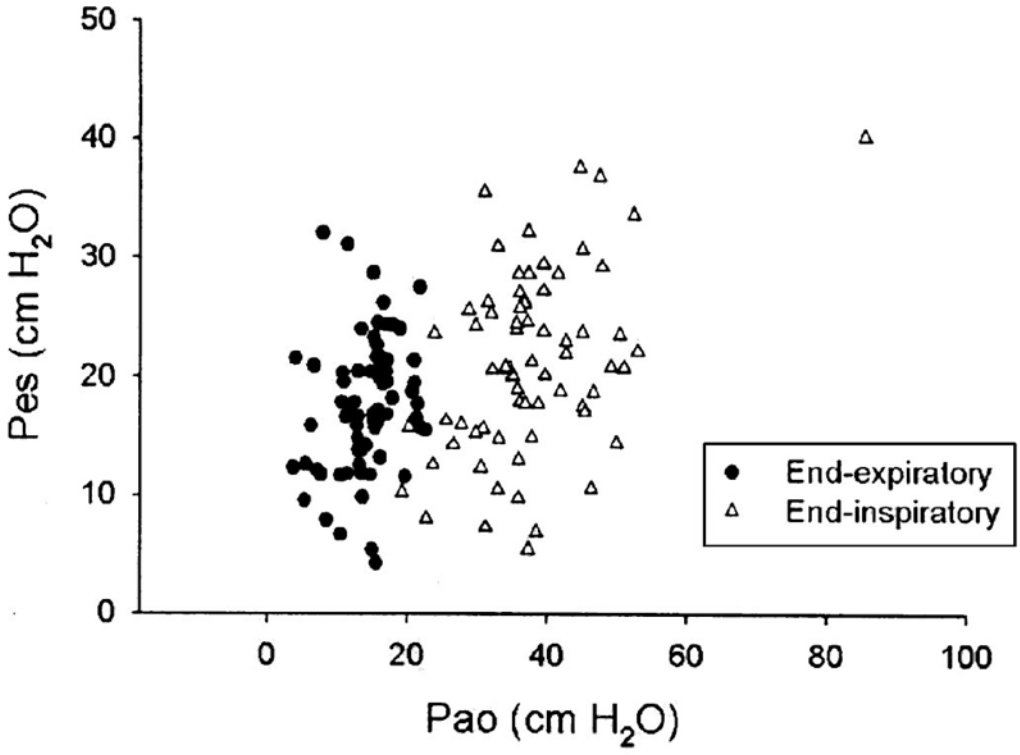

Figure 2.
Esophageal pressures (P_{es}) as a function of airway pressure (P_{ao}). P_{es} was not significantly correlated with P_{ao} at end-expiration ($R^2 = .054$, $p = .055$) but it was at end-inspiration ($R^2 = .188$, $p = .0002$).

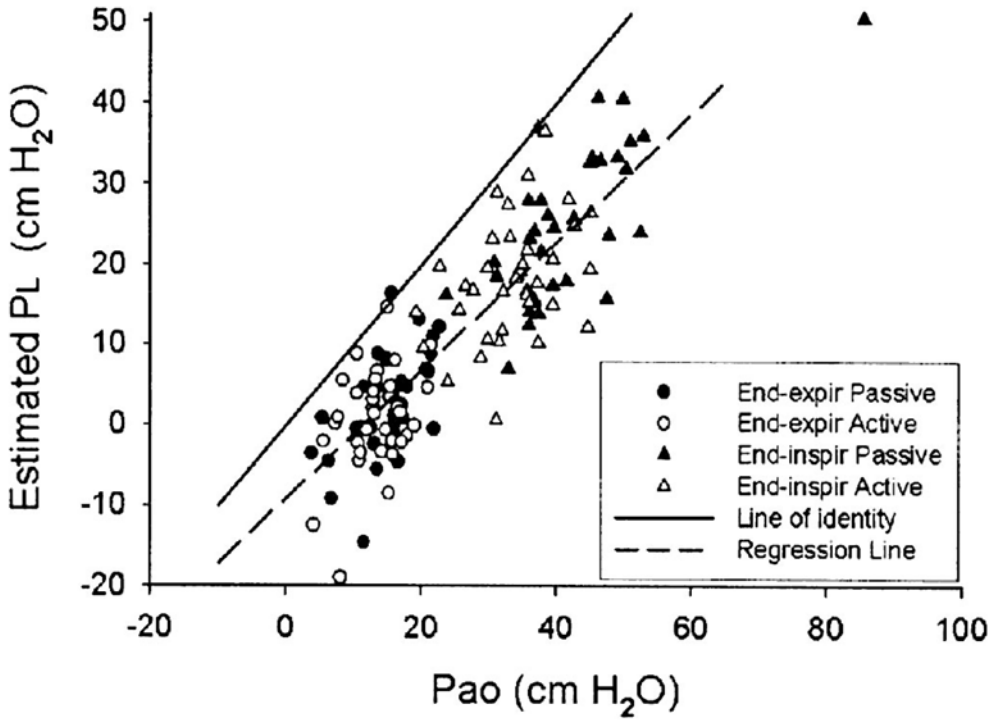

Figure 3.

The relationship between estimated transpulmonary pressure (P_L) and pressure at the airway opening (P_{ao}). P_L was correlated with P_{ao} both at end-expiration ($R^2 = .243$, $p < .0001$) and end-inspiration ($R^2 = .45$, $p < .0001$). There was, however, an inconsistent and unpredictable underestimation of P_L by the P_{ao} as evidenced by the offset from the line of identity. P_L at end-inflation was higher in passively ventilated patients than in those making active respiratory efforts, possibly because sicker patients with stiffer lungs were more likely to be deeply sedated or paralyzed and thus passive.

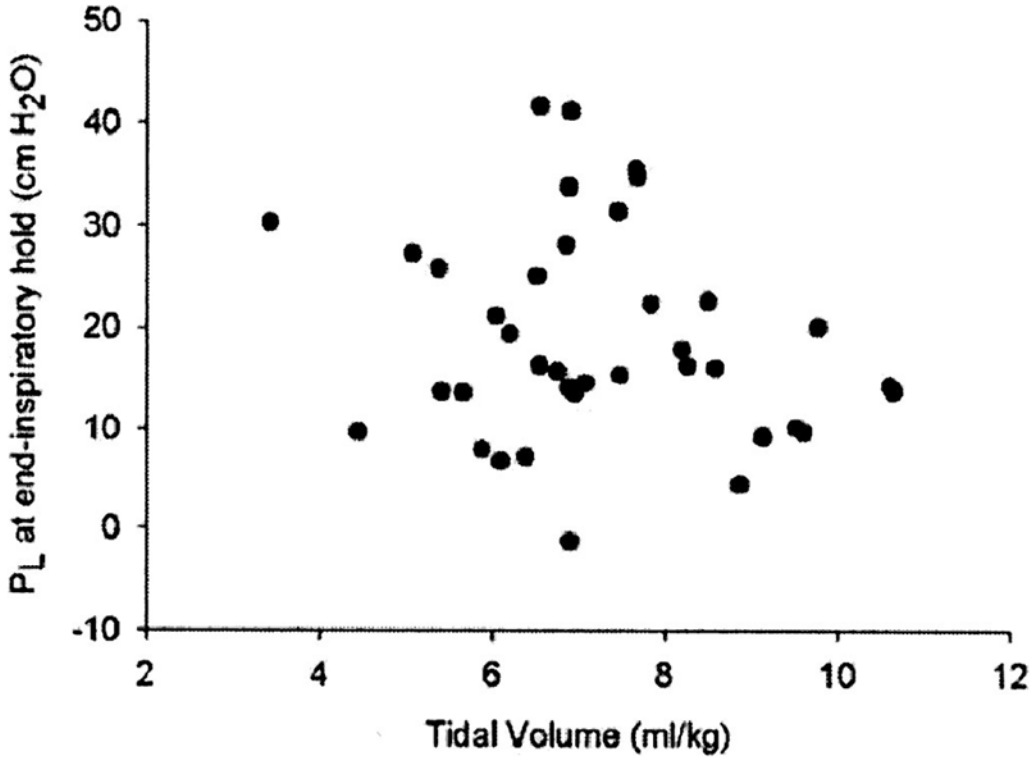

Figure 4.
Transpulmonary pressure (P_L) at the end-inspiratory hold as a function of tidal volume. There was no significant correlation.

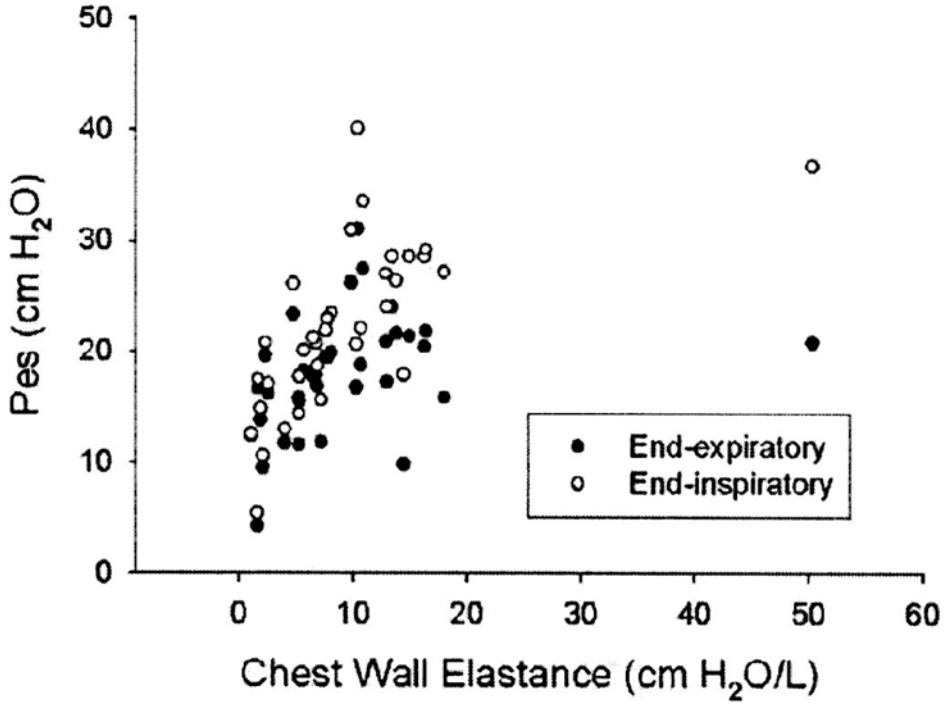

Figure 5.

Esophageal pressure (P_{es}) as a function of chest wall elastance. P_{es} at end-expiration was not significantly correlated with stiffness of the chest wall as estimated by chest wall elastance from P_{es} at zero flow during tidal ventilation ($R^2 = .011$, $p = .05$), although P_{es} at end-inflation was ($R^2 = .43$, $p < .0001$).

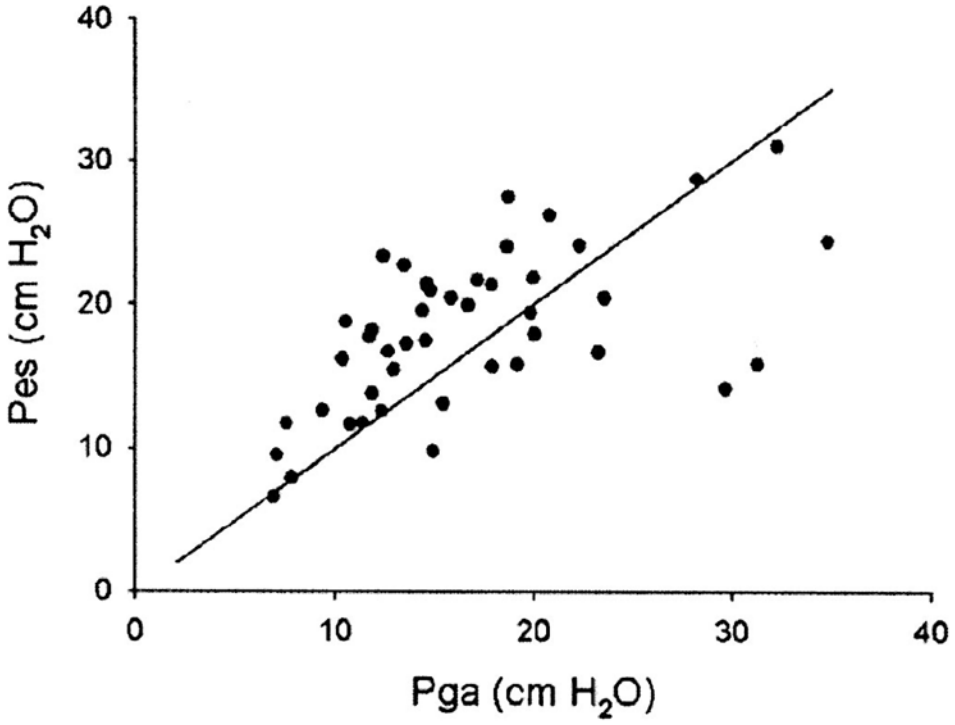

Figure 6.
The relationship between esophageal pressure (P_{es}) and gastric pressure (P_{ga}). Esophageal pressure at end-expiration was significantly correlated with Pga ($R^2 = .354$, $p < .0001$).

Table 1

Baseline patient characteristics

Characteristic	Values
Total patients	70
Males, n (%)	44 (62.9)
BMI (SD)	31 (10)
Age, yrs (SD)	54 (16)
Hospital LOS, days (SD)	27 (17)
ICU LOS, days (SD)	23 (16)
Ventilator days (SD)	20 (14)
Mortality, n (%)	20 (28.2)
Ventilator settings	
Tidal volume, mL (SD)	487 (124)
Tidal volume/IBW, mL/kg (SD)	7.4 (1.9)
Respiratory rate, min^{-1} (SD)	25.1 (13.6)
PEEP, cm H_2O (SD)	14.2 (4.5)
Plateau pressure, cm H_2O (SD)	36.4 (7.1)
Diagnoses/ARDS risk factors, n (%)	
Sepsis	34 (48.6)
Pneumonia	30 (42.9)
Trauma/surgery	25 (35.7)
Aspiration	14 (20.0)
Pancreatitis	13 (18.6)
Liver failure	9 (12.9)
Hematological/transfusions	17 (24.3)

BMI, body mass index; LOS, length of stay; ICU, intensive care unit; IBW, ideal body weight; PEEP, positive end-expiratory pressure; ARDS, acute respiratory distress syndrome.