

# Transpulmonary pressure measurement

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## Effect of Titrating Positive End-Expiratory Pressure (PEEP) With an Esophageal Pressure-Guided Strategy vs an Empirical High PEEP-Fio2 Strategy on Death and Days Free From Mechanical Ventilation Among Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial

Beitler JR, Sarge T, Banner-Goodspeed VM, Gong MN, Cook D, Novack V, Loring SH, Talmor D; EPVent-2 Study Group

JAMA. 2019 Mar 5;321(9):846-857

PMID 30776290, <http://www.ncbi.nlm.nih.gov/pubmed/30776290>

<b>Design</b>	Phase 2 multicenter randomized controlled trial
<b>Patients</b>	200 patients with moderate to severe Advanced Respiratory Distress Syndrome (ARDS): 102 in esophageal pressure-guided PEEP group, 98 in empirical high PEEP-fraction of inspired oxygen (FiO2) group
<b>Objectives</b>	Determine whether PEEP titration guided by esophageal pressure (Pes) is more effective than empirical high PEEP-FiO2 in moderate to severe ARDS patients
<b>Main Results</b>	The primary composite end point (ranked composite score incorporating death and days free from mechanical ventilation among survivors through day 28) was not different between the treatment groups. At 28 days, 33 patients in the Pes group and 30 patients in the empirical high PEEP-FiO2 group died. Days free from mechanical ventilation among survivors was not significantly different. Patients assigned to Pes-guided PEEP were significantly less likely to receive rescue therapy.
<b>Conclusion</b>	Among patients with moderate to severe ARDS, Pes-guided PEEP compared with empirical high PEEP-FiO2 resulted in no significant difference in outcomes.
<b>Comment</b>	The difference between this study and the first EPvent study was the PEEP in the control group, which was at a higher level in this study. This leads to positive end-expiratory transpulmonary pressure in the control group and the same level of driving pressure in both groups.

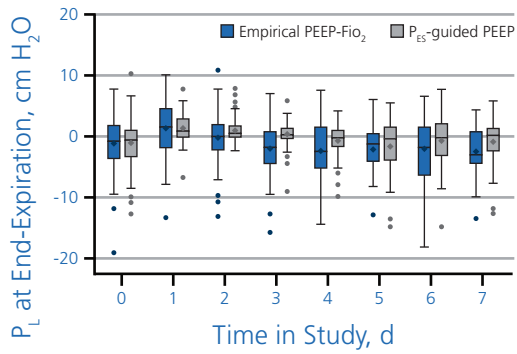


Figure 1: Pes and empirical methods achieved the same level of pressure

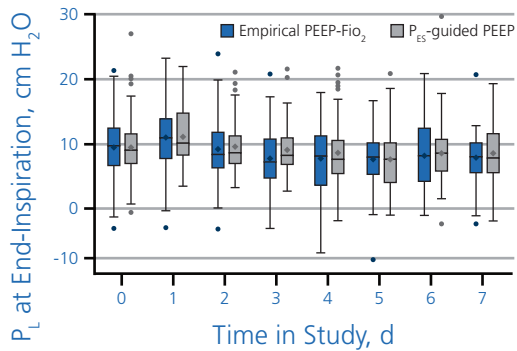


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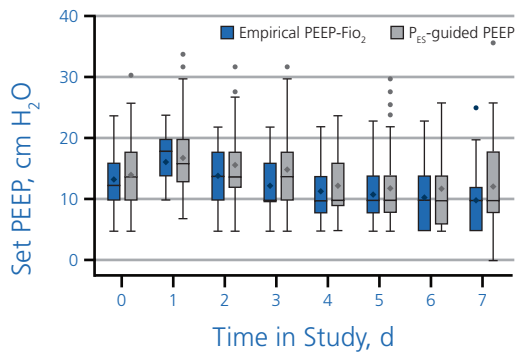


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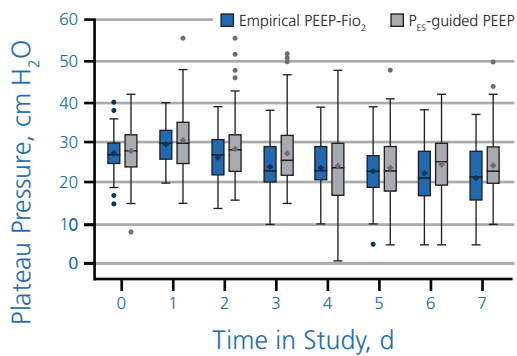


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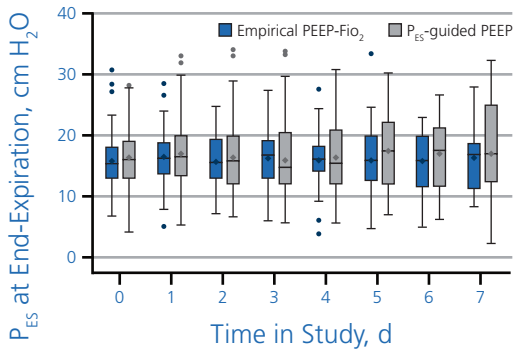


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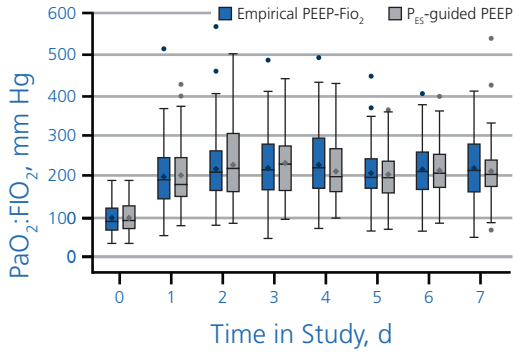


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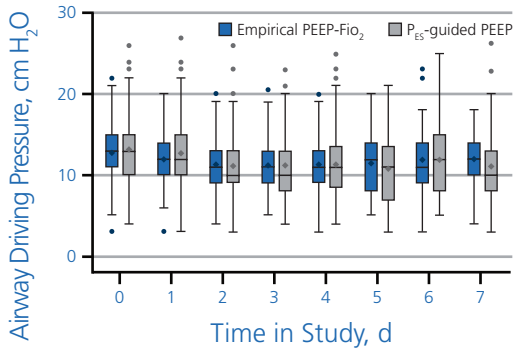


Figure 1: Pes and empirical methods achieved the same level of pressure

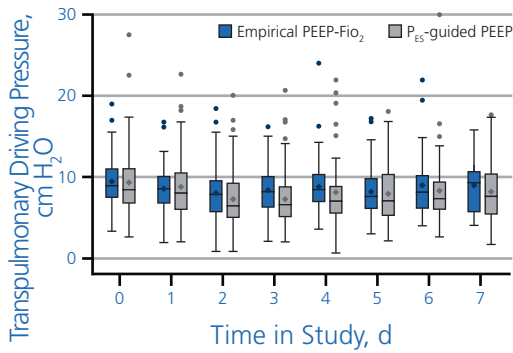


Figure 1: Pes and empirical methods achieved the same level of pressure

## Esophageal Manometry and Regional Transpulmonary Pressure in Lung Injury

Yoshida T, Amato MBP, Grieco DL, Chen L, Lima CAS, Roldan R, Morais CCA, Gomes S, Costa ELV, Cardoso PFG, Charbonney E, Richard JM, Brochard L, Kavanagh BP

Am J Respir Crit Care Med. 2018 Apr 15;197(8):1018-1026

PMID 29323931, <http://www.ncbi.nlm.nih.gov/pubmed/29323931>

<b>Design</b>	Animal and experimental study
<b>Patients</b>	6 lung-injured pigs and 3 human cadavers
<b>Objectives</b>	Determine the accuracy of esophageal pressure (Pes) and in which regions esophageal manometry reflects pleural pressure (Ppl) and transpulmonary pressure (PL); to assess whether lung stress in nondependent regions can be estimated at end-inspiration from PL
<b>Main Results</b>	Inspiratory and expiratory PL using Pes closely reflected values in the dependent to middle lung (adjacent to the esophagus). Inspiratory PL estimated from the elastance ratio reflected the directly measured nondependent values.
<b>Conclusion</b>	Expiratory PL derived from Pes reflects PL in the dependent to middle lung, where atelectasis usually predominates; inspiratory PL estimated from elastance ratio may indicate the highest level of lung stress in nondependent "baby" lung, where it is vulnerable to ventilator-induced lung injury.

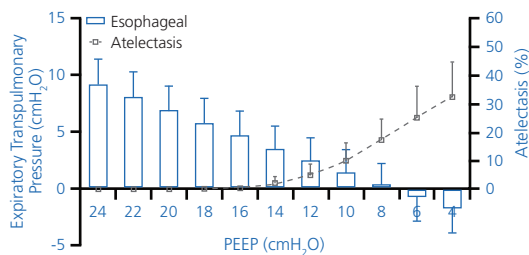


Figure 9: Atelectasis increased when expiratory PL decreased

## Effects of neuromuscular blockers on transpulmonary pressures in moderate to severe acute respiratory distress syndrome

Guervilly C, Bisbal M, Forel JM, Mechat M, Lehingue S, Bourenne J, Perrin G, Rambaud R, Adda M, Hraiech S, Marchi E, Roch A, Gainnier M, Papazian L

Intensive Care Med. 2017 Mar;43(3):408-418

PMID 28013329, <http://www.ncbi.nlm.nih.gov/pubmed/28013329>

<b>Design</b>	Prospective randomized controlled study
<b>Patients</b>	30 patients with moderate (13 in neuromuscular blocking agents (NMBA) group, 11 in control group) to severe (6, all with NMBA) acute respiratory distress syndrome (ARDS)
<b>Objectives</b>	Investigate whether NMBA exert beneficial effects in ARDS by reason of their action on respiratory mechanics, particularly transpulmonary pressure (PL)
<b>Main Results</b>	NMBA infusion was associated with an improvement in oxygenation in both moderate and severe ARDS, accompanied by a decrease in both plateau pressure and total positive end-expiratory pressure. Mean inspiratory and expiratory PL were higher in the moderate ARDS group receiving NMBA than in the control group. There was no change in either driving pressure or $\Delta$ PL related to NMBA administration.
<b>Conclusion</b>	NMBA exert beneficial effects in patients with ARDS, with potent favorable effects on PL.

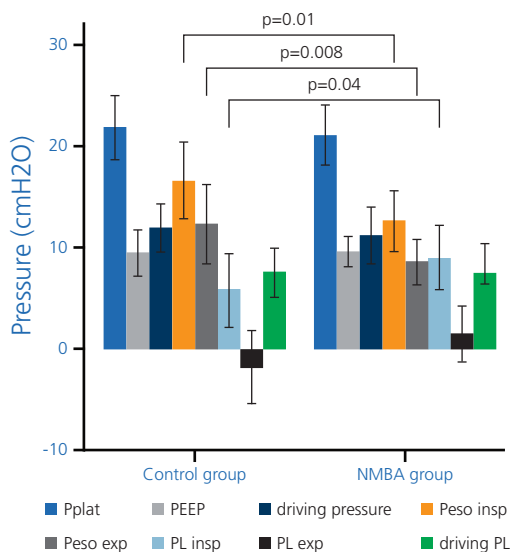


Figure 10: Comparison of pressures between NMBA and control groups



# Mortality and pulmonary mechanics in relation to respiratory system and transpulmonary driving pressures in ARDS

Baedorf Kassis E, Loring SH, Talmor D

Intensive Care Med. 2016 Aug;42(8):1206-13

PMID 27318943, <http://www.ncbi.nlm.nih.gov/pubmed/27318943>

<b>Design</b>	EPVent substudy
<b>Patients</b>	56 patients from the previous EPVent study (comparisons between survivors and non-survivors according to randomized groups)
<b>Objectives</b>	Examine the relationships between respiratory system and transpulmonary driving pressure, pulmonary mechanics at baseline, 5 min and 24 h, and 28-day mortality
<b>Main Results</b>	At baseline and 5 min there was no difference in respiratory system or transpulmonary driving pressure. By 24 h, survivors had lower respiratory system and transpulmonary driving pressures and the intervention group had lower transpulmonary driving pressure.
<b>Conclusion</b>	Targeting positive transpulmonary pressure improved elastance and driving pressures, and may be associated with improved 28 day mortality

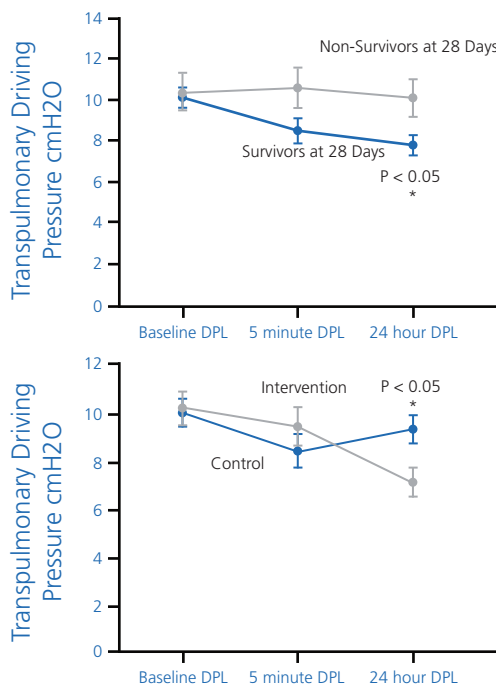


Figure 11: Survivors and patients in the intervention group had lower transpulmonary driving pressures

## Mechanical ventilation guided by esophageal pressure in acute lung injury

Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, Novack V, Loring SH

N Engl J Med. 2008 Nov 13;359(20):2095-104

PMID 19001507, <http://www.ncbi.nlm.nih.gov/pubmed/19001507>

**Design** RCT: PEEP adjusted according to measurements of  $P_{\text{es}}$  (esophageal pressure) to reach a positive end-expiratory  $P_{\text{tp}}$  (transpulmonary pressure) or according to the ARDS Network table EPVent trial

**Patients** 61 ALI/ARDS patients

**Objectives** Compare the oxygenation, compliance, and outcomes

**Main Results**  $\text{PaO}_2/\text{FiO}_2$  at 72 h was 88 mmHg higher in the esophageal-pressure-guided group than in the control group. This effect was observed at 24, 48, and 72 h. Respiratory-system compliance was significantly better at 24, 48, and 72 h in the esophageal-pressure-guided group. The study reached its stopping criterion and was terminated after 61 patients had been enrolled, so the outcomes were not different between groups.

**Conclusion** Target positive end expiratory  $P_{\text{tp}}$  improved oxygenation and compliance in ARDS patients

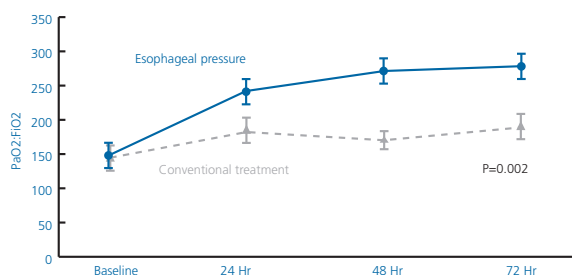
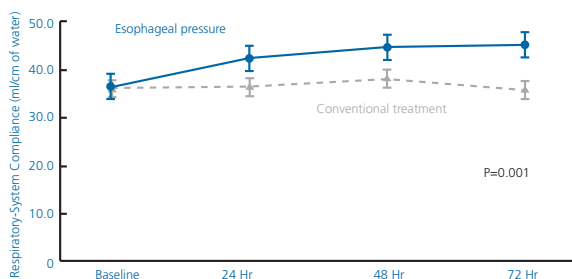


Figure 12: Target positive end expiratory  $P_{\text{tp}}$  increased PF ratio and  $C_{\text{rs}}$  (compliance of respiratory system) significantly



## Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome

Chiumello D, Carlesso E, Cadringer P, Caironi P, Valenza F, Polli F, Tallarini F, Cozzi P, Cressoni M, Colombo A, Marini JJ, Gattinoni L

Am J Respir Crit Care Med. 2008 Aug 15;178(4):346-55

PMID 18451319, <http://www.ncbi.nlm.nih.gov/pubmed/18451319>

<b>Design</b>	Prospective interventional comparative study
<b>Patients</b>	80 ICU patients: 40 ALI/ARDS, 40 controls
<b>Objectives</b>	Determine whether Pplat (plateau pressure) is an adequate surrogate for stress quantitatively equal to $\Delta P_{tp}$ (transpulmonary pressure)
<b>Main Results</b>	A given applied $\Delta P_{aw}$ (airway pressure) produced largely variable stress due to the variability of the EI (elastance of lung)/Ers. (elastance of respiratory system) Patients with ALI/ARDS reached higher $\Delta P_{tp}$ than the control group.
<b>Conclusion</b>	Pplat was an inadequate surrogate for lung stress

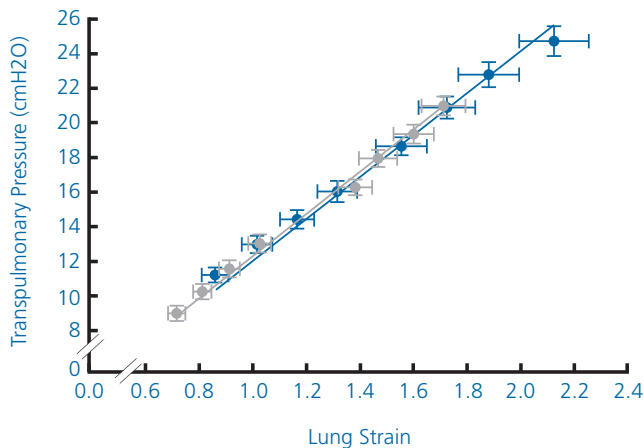


Figure 13: Stress and strain were linked by a constant proportionality factor. Knowing one, we can deduce the other.

## Esophageal and transpulmonary pressures in acute respiratory failure

Talmor D, Sarge T, O'Donnell CR, Ritz R, Malhotra A, Lisbon A, Loring SH

Crit Care Med. 2006 May;34(5):1389-94

PMID 16540960, <http://www.ncbi.nlm.nih.gov/pubmed/16540960>

<b>Design</b>	Prospective observational study
<b>Patients</b>	70 patients with ARF
<b>Objectives</b>	Characterize influence of the chest wall on Ptp (transpulmonary pressure) at end expiration and end inspiration
<b>Main Results</b>	Peso (esophageal pressure) averaged $17.5 \pm 5.7$ cmH <sub>2</sub> O at end expiration and $21.2 \pm 7.7$ cmH <sub>2</sub> O at end inspiration. Peso was not significantly correlated with BMI. Ptp (transpulmonary pressure) was $1.5 \pm 6.3$ cmH <sub>2</sub> O at end expiration, $21.4 \pm 9.3$ cmH <sub>2</sub> O at end inspiration, and $18.4 \pm 10.2$ cmH <sub>2</sub> O during a plateau, Ptp at end expiration was correlated with PEEP ( $p < .0001$ ). 24% of the variance in Ptp was explained by Paw (airway pressure) ( $R = .243$ ), 52% was due to variation in Peso.
<b>Conclusion</b>	Elevated Peso suggested that chest wall mechanical properties contribute substantially and unpredictably to the respiratory system, and therefore, Paw did not adequately predict Ptp or lung distention

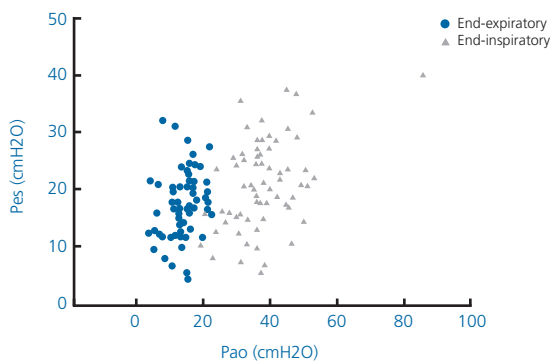


Figure 14: Paw could not predict the esophageal pressure

## Effect of Esophageal Pressure-guided Positive End-Expiratory Pressure on Survival from Acute Respiratory Distress Syndrome: A Risk-based and Mechanistic Reanalysis of the EPVent-2 Trial

Sarge T, Baedorf-Kassis E, Banner-Goodspeed V, Novack V, Loring SH, Gong MN, Cook D, Talmor D, Beitler JR; EPVent-2 Study Group

2021 Nov 15;204(10):1153-1163

PMID 34464237, <http://www.ncbi.nlm.nih.gov/pubmed/34464237>

<b>Design</b>	Post-hoc reanalysis of the EPVent-2 trial evaluated for heterogeneity of treatment effect on mortality by baseline multiorgan dysfunction, determined via APACHE-II score
<b>Patients</b>	200 trial participants
<b>Objectives</b>	Evaluate whether multiorgan dysfunction and lung mechanics modified treatment effect in the EPVent-2 trial and whether PEEP titrated to end-expiratory transpulmonary pressure near 0 cmH <sub>2</sub> O was associated with survival
<b>Main Results</b>	Treatment effect on 60-day mortality differed by multiorgan dysfunction severity (P = 0.03). Pes-guided PEEP was associated with lower mortality among patients with an APACHE-II score lower than the median value and may have had the opposite effect in patients with a higher APACHE-II score. Independent of treatment group or multiorgan dysfunction severity, mortality was lowest when PEEP titration achieved end-expiratory transpulmonary pressure near 0 cmH <sub>2</sub> O.
<b>Conclusion</b>	The effect on survival of Pes-guided PEEP, compared with empirical high PEEP, differed by multiorgan dysfunction severity. Independent of multiorgan dysfunction, PEEP titrated to end-expiratory transpulmonary pressure closer to 0 cmH <sub>2</sub> O was associated with greater survival than more positive or negative values

## Transpulmonary pressure measurements and lung mechanics in patients with early ARDS and SARS-CoV-2

Baedorf Kassis E, Schaefer MS, Maley JH, Hoenig B, Loo Y, Hayes MM, Moskowitz A, Talmor D

J Crit Care. 2021 Jun;63:106-112

PMID 33676795, <http://www.ncbi.nlm.nih.gov/pubmed/33676795>

<b>Design</b>	Observational study
<b>Patients</b>	40 patients with confirmed SARS-CoV-2 and ARDS
<b>Objectives</b>	Describe lung, chest-wall and respiratory-system mechanics in patients with SARS-CoV-2 and ARDS
<b>Main Results</b>	Respiratory-system (30–35 ml/cm H <sub>2</sub> O), lung (40–50 ml/cm H <sub>2</sub> O) and chest-wall (120–150 ml/cm H <sub>2</sub> O) compliance remained similar over the first week. Elevated basal pleural pressures correlated with BMI. Patients required prolonged mechanical ventilation (14.5 days [9.50–19.0]), with a mortality of 32.5%.
<b>Conclusion</b>	Patients with ARDS caused by SARS-CoV-2 displayed normal chest-wall mechanics, with increased basal pleural pressure. Respiratory system and lung mechanics were similar to known existing ARDS cohorts. The wide range of respiratory system mechanics illustrates the inherent heterogeneity that is consistent with typical ARDS

## Reverse Trigger Phenotypes in Acute Respiratory Distress Syndrome

Baedorf Kassis E, Su HK, Graham AR, Novack V, Loring SH, Talmor DS

Am J Respir Crit Care Med. 2021 Jan 1;203(1):67-77

PMID 32809842, <http://www.ncbi.nlm.nih.gov/pubmed/32809842>

<b>Design</b>	Retrospective observational study
<b>Patients</b>	55 patients with ARDS
<b>Objectives</b>	Retrospectively identify reverse trigger phenotypes and characterize their impacts on Vt and transpulmonary pressure. Four phenotypes of reverse triggering with and without breath-stacking and their impact on lung inflation and deflation were investigated.
<b>Main Results</b>	Reverse triggering was detected in 25 patients, 15 with associated breath stacking, and 13 with stable reverse triggering consistent with respiratory entrainment. Phenotypes were associated with variable levels of inspiratory effort. Early reverse triggering with early expiratory relaxation increased tidal volume and inspiratory transpulmonary pressures compared with passive breaths. Early reverse triggering with delayed expiratory relaxation increased tidal volume and increased inspiratory and mean-expiratory transpulmonary pressure. Mid-cycle reverse triggering (initiation during inflation and maximal effort during deflation) increased tidal volume, increased inspiratory and mean-expiratory transpulmonary pressure, and caused incomplete exhalation. Late reverse triggering (occurring exclusively during exhalation) increased mean expiratory transpulmonary pressure and caused incomplete exhalation. Breath-stacking resulted in large delivered volumes.
<b>Conclusion</b>	Reverse triggering causes variable physiological effects, depending on the phenotype. Differentiating between phenotype effects may be important to understand the clinical impacts of these events

## Effects of positive end-expiratory pressure strategy in supine and prone position on lung and chest wall mechanics in acute respiratory distress syndrome

Mezidi M, Parrilla FJ, Yonis H, Riad Z, Böhm SH, Waldmann AD, Richard JC, Lissonde F, Tapponnier R, Baboi L, Mancebo J, Guérin C

Ann Intensive Care. 2018 Sep 10;8(1):86

PMID 30203117, <http://www.ncbi.nlm.nih.gov/pubmed/30203117>

<b>Design</b>	Prospective physiological study
<b>Patients</b>	38 patients with acute respiratory distress syndrome (ARDS) with PaO <sub>2</sub> /FIO <sub>2</sub> < 150 mmHg, randomized to receive esophageal pressure-guided positive end-expiratory pressure (PEEP) or PEEP according to a PEEP/FIO <sub>2</sub> table in prone position
<b>Objectives</b>	Compare an esophageal pressure (Pes) guided strategy to set PEEP in supine (SP) and in prone position (PP) with a PEEP/FIO <sub>2</sub> table and explore the early (1 h) and late (16 h) effects of PP on lung and chest wall mechanics
<b>Main Results</b>	In SP, PEEP in the Pes-guided group was higher compared to the PEEP/FIO <sub>2</sub> table (10 ± 2 versus 12 ± 4 cmH <sub>2</sub> O). There was no difference in PP. With the Pes-guided strategy, chest wall elastance increased regardless of position. Lung elastance and transpulmonary driving pressure decreased in PP, with no effect of PEEP strategy. Both PP and the Pes-guided strategy improved oxygenation. End-expiratory lung volume (EELV) did not change with the PEEP strategy. At the end of the PP session, respiratory mechanics did not vary, but EELV and PaO <sub>2</sub> /FIO <sub>2</sub> increased, while PaCO <sub>2</sub> decreased.
<b>Conclusion</b>	There was no impact of PP on Pes measurements. PP had an immediate improvement effect on lung mechanics and a late lung recruitment effect independent of PEEP strategy.



## Effects of Prone Positioning on Transpulmonary Pressures and End-expiratory Volumes in Patients without Lung Disease

Kumaresan A, Gerber R, Mueller A, Loring SH, Talmor D

Anesthesiology. 2018 Jun;128(6):1187-1192

PMID 29521672, <http://www.ncbi.nlm.nih.gov/pubmed/29521672>

<b>Design</b>	Prospective physiological study
<b>Patients</b>	16 patients undergoing spine surgery during general anesthesia and neuromuscular blockade
<b>Objectives</b>	Characterize effects of prone positioning (PP) on esophageal pressure, transpulmonary pressure, and lung volume
<b>Main Results</b>	End-expiratory esophageal pressure with ZEEP decreased from SP to PP by 6 cmH <sub>2</sub> O. End-expiratory lung volume increased from SP to PP by 0.15 l. Chest wall elastance increased from SP to PP by 7 cmH <sub>2</sub> O/l at ZEEP and 7 cmH <sub>2</sub> O/l at PEEP 7 cmH <sub>2</sub> O. Driving pressure increased in PP at ZEEP and PEEP 7cmH <sub>2</sub> O.
<b>Conclusion</b>	In PP, end-expiratory esophageal pressure, end-expiratory transpulmonary pressure and end-expiratory lung volume increased. Driving pressure increased in PP due to increased chest wall elastance.

## Recruitment maneuvers: using transpulmonary pressure to help Goldilocks

Baedorf Kassis E, Loring SH, Talmor D

Intensive Care Med. 2017 Aug;43(8):1162-1163

PMID 28386726, <http://www.ncbi.nlm.nih.gov/pubmed/28386726>

<b>Design</b>	Post hoc analysis
<b>Patients</b>	28 patients with acute respiratory distress syndrome (ARDS)
<b>Objectives</b>	Evaluate if recruitment maneuvers targeting airway pressures result in unpredictable transpulmonary pressure (PL), causing either under-recruitment or overdistension
<b>Main Results</b>	Recruitment maneuvers resulted in unpredictable transpulmonary pressure. Recruitment volume (VRM) was dependent on transpulmonary pressure. Larger VRM is attained in "recruitable" lungs, regardless of baseline elastance. High recruitment transpulmonary pressure causes overdistension. Change in lung volume ( $\Delta EL$ ) was positive during recruitment in patients with recruitment transpulmonary pressure (PL, RM) $\geq 20$ cmH <sub>2</sub> O and negative in those with PL, RM $< 20$ cmH <sub>2</sub> O, suggesting a safety threshold of 20 cmH <sub>2</sub> O to avoid overdistension. $\Delta EL$ was negligible in patients with PL, RM below 10 cmH <sub>2</sub> O, while $\Delta EL$ was negative when PL, RM was between 10 and 20 cmH <sub>2</sub> O.
<b>Conclusion</b>	The optimal peak transpulmonary pressure during recruitment, where pressure expands the lung, optimizes elastance, and avoids overdistension, is between 10 and 20 cmH <sub>2</sub> O.
<b>Comment</b>	This analysis is presented in the form of a letter because there are only few results, but the findings are very important.

## Recruitment maneuvers and positive end-expiratory pressure titration in morbidly obese ICU patients.

Pirrone M, Fisher D, Chipman D, Imber DA, Corona J, Mietto C, Kacmarek RM, Berra L

Crit Care Med. 2016 Feb;44(2):300-7

PMID 26584196, <http://www.ncbi.nlm.nih.gov/pubmed/26584196>

<b>Design</b>	Prospective, crossover, nonrandomized interventional study
<b>Patients</b>	14 ventilated morbidly obese (body mass index > 35 kg/m <sup>2</sup> ) ICU patients
<b>Objectives</b>	Compare PEEP set by the clinician, PEEP set according to positive end expiratory transpulmonary pressure, and PEEP associated with the least driving pressure, before and after a staircase recruitment maneuver
<b>Main Results</b>	Both methods identified similar optimal PEEP (21 ±4 vs 21 ±4cmH <sub>2</sub> O; p = 0.40). PEEP increased end-expiratory lung volume (Δ11 ±7mL/kg; p<0.01) and oxygenation (Δ86 ±50torr; p<0.01) and decreased elastance of the lung (Δ5±5 cmH <sub>2</sub> O/l; p<0.01). Recruitment maneuvers were effective at increasing EELV (end-expiratory lung volume) and decreasing end-inspiratory transpulmonary pressure, suggesting an improved distribution of lung aeration and reduction of overdistension. PEEP set by the clinicians (12 ±3 cmH <sub>2</sub> O) were associated with lower lung volumes, worse elastic properties of the lung, and lower oxygenation.
<b>Conclusion</b>	Recruitment maneuvers followed by PEEP titration improved lung volumes, respiratory system elastance, and oxygenation compared with PEEP commonly set by the clinician in morbidly obese patients

## Volume delivered during recruitment maneuver predicts lung stress in acute respiratory distress syndrome

Beitler JR, Majumdar R, Hubmayr RD, Malhotra A, Thompson BT, Owens RL, Loring SH, Talmor D

Crit Care Med. 2016 Jan;44(1):91-9

PMID 26474111, <http://www.ncbi.nlm.nih.gov/pubmed/26474111>

<b>Design</b>	EPVent substudy
<b>Patients</b>	42 ARDS patients
<b>Objectives</b>	Determine whether the volume delivered during a recruitment maneuver (VRM), consisting of sustained inflation at 40 cmH <sub>2</sub> O for 30 s, is inversely associated with lung stress and mortality in acute respiratory distress syndrome
<b>Main Results</b>	VRM ranged between 7.4 and 34.7 ml/kg predicted body weight. Lower VRM predicted high end-inspiratory and tidal lung stress. Low VRM was also associated with an increased risk of death.
<b>Conclusion</b>	Low VRM predicted high lung stress and may predict risk of death in patients with acute respiratory distress syndrome

## Effect of body mass index in acute respiratory distress syndrome

Chiumello D, Colombo A, Algieri I, Mietto C, Carlesso E, Crimella F, Cressoni M, Quintel M, Gattinoni L

Br J Anaesth. 2016 Jan;116(1):113-21

PMID 26675954, <http://www.ncbi.nlm.nih.gov/pubmed/26675954>

<b>Design</b>	Prospective physiological study
<b>Patients</b>	101 ARDS patients
<b>Objectives</b>	Compare respiratory mechanics between normal-weight and obese ARDS patients
<b>Main Results</b>	Obese, overweight, and normal-weight groups presented a similar EI (elastance of lung) and Ecw (elastance of chest wall) at 5 and 15 cmH <sub>2</sub> O of PEEP. Lung recruitability was not affected by the body weight. Lung gas volume was significantly lower whereas the total superimposed pressure (representing PTP to be applied at end expiration to counterbalance the increased lung weight and to keep open whatever lung units had opened at the previous inspiration) was significantly higher in the obese compared with the normal-weight group.
<b>Conclusion</b>	Obese ARDS patients do not present higher chest wall elastance and lung recruitability

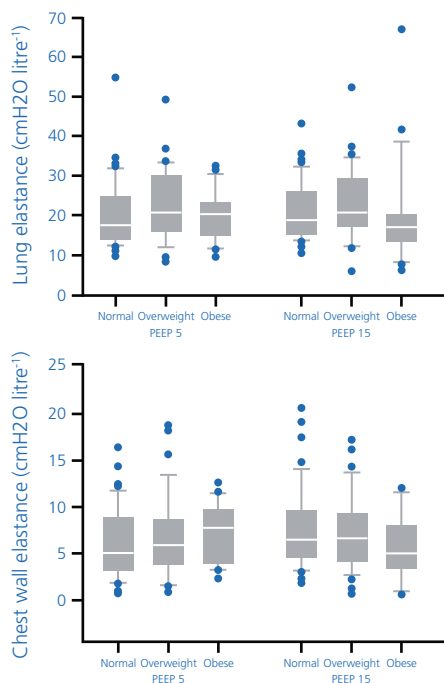


Figure 15: Results showed no difference between the weight groups with respect to lung and chest wall elastance at 2 different PEEP levels

# Transpulmonary pressure and gas exchange during decremental PEEP titration in pulmonary ARDS patients

Rodriguez PO, Bonelli I, Setten M, Attie S, Madorno M, Maskin LP, Valentini R

Respir Care. 2013 May;58(5):754-63

PMID 23051849, <http://www.ncbi.nlm.nih.gov/pubmed/23051849>

<b>Design</b>	Prospective interventional study
<b>Patients</b>	11 ARDS patients
<b>Objectives</b>	Describe Ptp (transpulmonary pressure) and gas exchange during a decremental PEEP trial
<b>Main Results</b>	End-expiratory Ptp became negative in all subjects when PEEP decreased below $8.9 \pm 5.2$ cmH2O. PaO2 decreased when expiratory Ptp became negative ( $p < 0.001$ ).
<b>Conclusion</b>	Negative end-expiratory Ptp indicated high risk of alveolar collapse and explained worse oxygenation

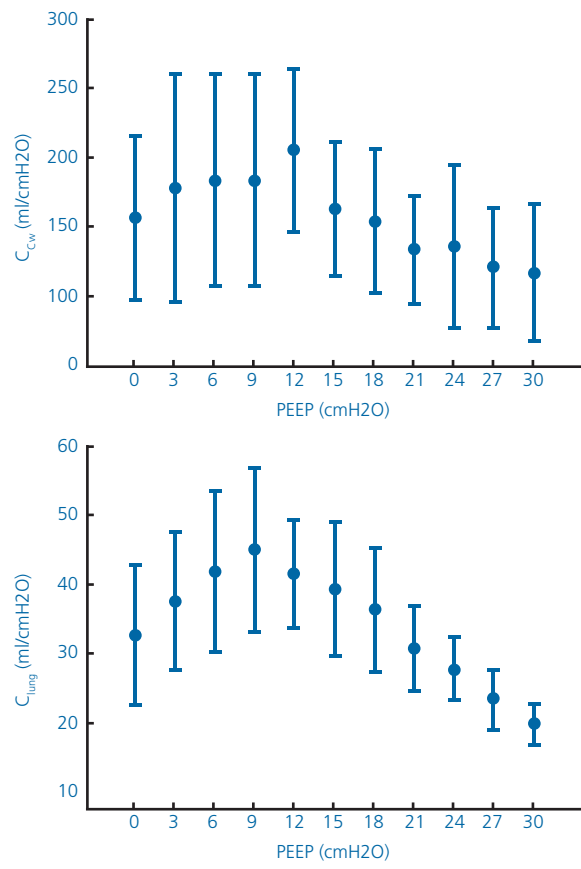


Figure 16: Cl (compliance of lung) was modified by the PEEP level while Ccw (compliance of chest wall) was not

## Acute respiratory distress syndrome caused by pulmonary and extrapulmonary disease. Different syndromes?

Gattinoni L, Pelosi P, Suter PM, Pedoto A, Vercesi P, Lissoni A

Am J Respir Crit Care Med. 1998 Jul;158(1):3-11

PMID 9655699, <http://www.ncbi.nlm.nih.gov/pubmed/9655699>

<b>Design</b>	Prospective interventional study
<b>Patients</b>	21 ICU patients: 12 patients with ARDS <sub>p</sub> , 9 with ARDS <sub>ex</sub>
<b>Objectives</b>	Assess the possible differences in respiratory mechanics between the ARDS originating from pulmonary disease (ARDS <sub>p</sub> ) and that originating from extrapulmonary disease (ARDS <sub>ex</sub> )
<b>Main Results</b>	At PEEP, Ers (elastance of respiratory system) and EELV (end-expiratory lung volume) were similar in both groups. El (elastance of lung) was higher in the ARDS <sub>p</sub> than in the ARDS <sub>ex</sub> (20.2 ±5.4 vs 13.8 ±5.0 cmH <sub>2</sub> O/L, p<0.05), Ecw (elastance of chest wall) was higher in the ARDS <sub>ex</sub> (12.1 ±3.8 vs 5.2 ±1.9 cmH <sub>2</sub> O/l, p<0.05). Intra abdominal pressure was higher in ARDS <sub>ex</sub> than in ARDS <sub>p</sub> (22.2 ±6.0 vs 8.5 ±2.9 cmH <sub>2</sub> O, p<0.01), and it significantly correlated with Ecw (p<0.01). Increasing PEEP to 15 cmH <sub>2</sub> O caused an increase of Ers in ARDS <sub>p</sub> (from 25.4 ±6.2 to 31.2 ±11.3 cmH <sub>2</sub> O/l, p<0.01) and a decrease in ARDS <sub>ex</sub> (from 25.9 ±5.4 to 21.4 ±5.5 cmH <sub>2</sub> O/l, p<0.01).
<b>Conclusion</b>	Pulmonary-sourced ARDS and extrapulmonary-sourced ARDS differ in the effect on lung vs. chest wall compliance and the response to PEEP. Eso (esophageal pressure) measurements allow for assessment of chest wall vs. pulmonary compliance and response to PEEP.

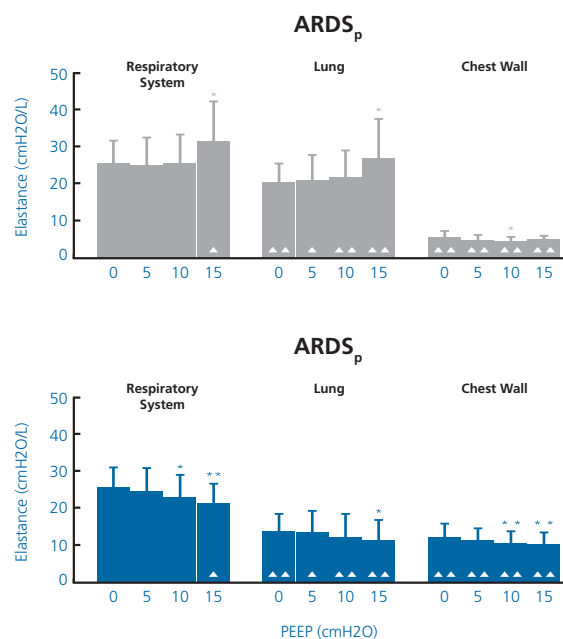


Figure 17: In pulmonary ARDS the Ers increase was due to increase of El. In extra pulmonary ARDS the Ers increase was due to increase of both Ecw and El.

# Alterations of lung and chest wall mechanics in patients with acute lung injury: effects of positive end-expiratory pressure

Pelosi P, Cereda M, Foti G, Giacomini M, Pesenti A

Am J Respir Crit Care Med. 1995 Aug;152(2):531-7

PMID 7633703, <http://www.ncbi.nlm.nih.gov/pubmed/7633703>

<b>Design</b>	Prospective interventional comparative study
<b>Patients</b>	24 ICU patients: 10 ALI, 8 ARDS, 8 controls
<b>Objectives</b>	Evaluate the individual contribution of chest wall and lungs to respiratory system mechanics
<b>Main Results</b>	At ZEEP, El (elastance of lung) and E <sub>cw</sub> (elastance of chest wall) were increased in patients with ALI and ARDS compared with control subjects. EELV (end-expiratory lung volume) was lower in ALI subjects than in control subjects, and much lower in ARDS patients.
<b>Conclusion</b>	In ALI/ARDS patients, not only El but also E <sub>cw</sub> increased

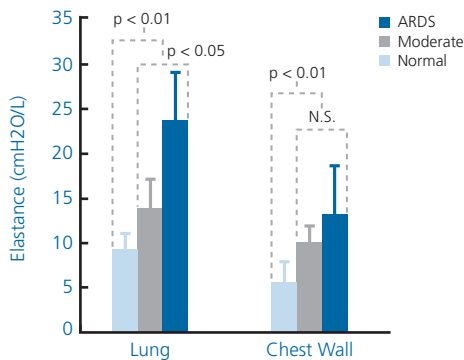


Figure 18: Elastance of both lungs and chest wall increase in ARDS



## Comparison of pleural and esophageal pressure in supine and prone positions in a porcine model of acute respiratory distress syndrome

Terzi N, Bayat S, Noury N, Turbil E, Habre W, Argaud L, Cour M, Louis B, Guérin C  
J Appl Physiol (1985). 2020 Jun 1;128(6):1617-1625  
PMID 32437245, <http://www.ncbi.nlm.nih.gov/pubmed/32437245>

<b>Design</b>	Animal study
<b>Patients</b>	6 pigs with severe ARDS
<b>Objectives</b>	Assess the relationship between Pes (esophageal pressure) and regional Ppl (pleural pressure) in supine and prone position at different levels of positive end-expiratory pressure (PEEP)
<b>Main Results</b>	Static end-expiratory esophageal pressure did not change significantly in prone position compared to supine position at any PEEP between 5 and 20 cmH2O. Prone position narrowed end-expiratory dorsal-to-ventral Ppl vertical gradient, likely because of a more even distribution of mechanical forces over the chest wall.
<b>Conclusion</b>	Prone position was associated with an increased ventral pleural pressure and reduced end-expiratory dorsal-to-ventral Ppl vertical gradient

## Impact of physician education and availability of parameters regarding esophageal pressure and transpulmonary pressure on clinical decisions involving ventilator management

Norisue Y, Ashworth L, Naito T, Kataoka J, Takeuchi M, Usami S, Takada J, Fujitani S  
J Crit Care. 2017 Oct;41:112-118  
PMID 28514715, <http://www.ncbi.nlm.nih.gov/pubmed/28514715>

<b>Design</b>	Prospective, before-after study using a case scenario-based questionnaire and a case simulator device
<b>Patients</b>	99 physicians
<b>Objectives</b>	Investigate the effects of physician education and the availability of esophageal pressure (Pes) and transpulmonary pressure (PL) data on physicians' decisions regarding ventilator management
<b>Main Results</b>	After receiving instructions and data on Pes and PL, statistically significant numbers of physicians changed their answers regarding ventilator management decisions in all five cases.
<b>Conclusion</b>	The use of case scenario-based education with simulator devices for physicians may hasten worldwide understanding and clinical application of Pes and PL.

## The occlusion tests and end-expiratory esophageal pressure: measurements and comparison in controlled and assisted ventilation

Chiumello D, Consonni D, Coppola S, Froio S, Crimella F, Colombo A

Ann Intensive Care. 2016 Dec;6(1):13

PMID 26868503, <http://www.ncbi.nlm.nih.gov/pubmed/26868503>

<b>Design</b>	Prospective physiological study
<b>Patients</b>	21 ICU patients
<b>Objectives</b>	Evaluate the effects of paralysis, two different esophageal balloon positions and two PEEP levels on the $\Delta P_{es}$ (esophageal pressure)/ $\Delta P_{aw}$ (airway pressure) ratio measured by the positive pressure occlusion and the Baydur tests and on the end-expiratory esophageal pressure and respiratory mechanics (lung and chest wall)
<b>Main Results</b>	The esophageal pressure/airway pressure ratio was slightly higher (+0.11) with the positive occlusion test compared with Baydur's test. The level of PEEP and the esophageal balloon position did not affect this ratio. The esophageal pressure and airway pressure were significantly related to a correlation coefficient of $r = 0.984$ during the Baydur test and $r = 0.909$ in the positive occlusion test. End-expiratory esophageal pressure was significantly higher in sedated and paralyzed patients compared with sedated patients (+2.47 cmH <sub>2</sub> O) and when esophageal balloon was positioned in the low position (+2.26 cmH <sub>2</sub> O). The esophageal balloon position slightly influenced the lung elastance, while the PEEP reduced the chest wall elastance without affecting the lung and total respiratory system elastance.
<b>Conclusion</b>	Paralysis and balloon position did not clinically affect the measurement of the esophageal pressure/airway pressure ratio, however they increased the end-expiratory esophageal pressure

## In vivo calibration of esophageal pressure in the mechanically ventilated patient makes measurements reliable

Mojoli F, Iotti GA, Torriglia F, Pozzi M, Volta CA, Bianzina S, Braschi A, Brochard L

Crit Care. 2016 Apr 11;20:98

PMID 27063290, <http://www.ncbi.nlm.nih.gov/pubmed/27063290>

<b>Design</b>	Prospective physiological study
<b>Patients</b>	36 patients
<b>Objectives</b>	Evaluate the feasibility and effectiveness of a calibration procedure consisting of optimizing balloon-filling and subtracting the pressure generated by the esophagus wall (Pew)
<b>Main Results</b>	VBEST (filling volume associated with the largest tidal increase of Pes) was $3.5 \pm 1.9$ ml (range 0.5-6.0). Esophagus elastance was $1.1 \pm 0.5$ cmH <sub>2</sub> O/ml. At filling volumes of 0.5 ml, VBEST and 4.0 ml respectively, Pew was $0.0 \pm 0.1$ , $2.0 \pm 1.9$ , and $3.0 \pm 1.7$ cmH <sub>2</sub> O ( $p < 0.0001$ ), whereas the occlusion test was satisfactory in 22%, 98%, and 88% of cases ( $p < 0.0001$ ).
<b>Conclusion</b>	Under mechanical ventilation, an increase of balloon filling above the conventionally recommended low volumes warranted complete transmission swings in esophageal pressure
<b>Comment</b>	A simple calibration procedure allows finding the filling volume associated with the best transmission of tidal Pes change and subtracting the associated baseline artifact, thus making measurement of absolute values of Pes reliable.

## Do spontaneous and mechanical breathing have similar effects on average transpulmonary and alveolar pressure? A clinical crossover study

Bellani G, Grasselli G, Teggia-Droghi M, Mauri T, Coppadoro A, Brochard L, Pesenti A

Crit Care. 2016 Apr 28;20(1):142

PMID 27160458, <http://www.ncbi.nlm.nih.gov/pubmed/27160458>

<b>Design</b>	Prospective crossover study
<b>Patients</b>	10 patients
<b>Objectives</b>	Compare the change in transpulmonary pressure between 3 levels of PSV (pressure support ventilation) and CMV (controlled mechanical ventilation), estimate the influence of SB (spontaneous breathing) on alveolar pressure, and determine whether a reliable plateau pressure could be measured during PSV
<b>Main Results</b>	Overall $\Delta P_{tp}$ (transpulmonary pressure) was similar between CMV and PSV, but some individual values were only loosely correlated. Spontaneous breathing acts on alveolar pressure in a similar way to PSV. Inspiratory occlusion holds performed during PSV measured $P_{plat}$ (plateau pressure) comparable to with CMV.
<b>Conclusion</b>	$\Delta P_{tp}$ was similar between CMV and PSV. Spontaneous breathing during mechanical ventilation can cause negative swings in alveolar pressure, a mechanism by which SB might potentially induce lung injury

## Non-invasive assessment of lung elastance in patients with acute respiratory distress syndrome

Garnero A, Tuxen D, Ducros L, Demory D, Donati SY, Durand-Gasselín J, Cooper J, Hodgson C, Arnal JM

Minerva Anesthesiol. 2015 Oct;81(10):1096-104

PMID 25424169, <http://www.ncbi.nlm.nih.gov/pubmed/25424169>

<b>Design</b>	Prospective physiological study
<b>Patients</b>	26 early onset, moderate to severe ARDS patients
<b>Objectives</b>	Compare lung elastance assessed by a noninvasive method called lung barometry (ELLB) versus esophageal pressure method (ELPeso)
<b>Main Results</b>	Concordance between ELLB and ELPeso using the Bland and Altman method demonstrated bias and large limits of agreement during the increase and decrease in PEEP. There was no linear correlation between ELLB/ERS and ELPeso/ERS during the increase and decrease in PEEP.
<b>Conclusion</b>	The lung barometry method cannot be used instead of the esophageal pressure measurement to assess lung elastance

## Positive end expiratory pressure titrated by transpulmonary pressure improved oxygenation and respiratory mechanics in acute respiratory distress syndrome patients with intra-abdominal hypertension

Yang Y, Li Y, Liu SQ, Liu L, Huang YZ, Guo FM, Qiu HB

Chin Med J. 2013;126(17):3234-9

PMID 24033942, <http://www.ncbi.nlm.nih.gov/pubmed/24033942>

<b>Design</b>	Prospective interventional study
<b>Patients</b>	15 ARDS patients: 7 with intra-abdominal hypertension (IAH, P <sub>blad</sub> >12 cmH <sub>2</sub> O), 8 without IAH
<b>Objectives</b>	Determine the effect of setting PEEP with P <sub>tp</sub> (transpulmonary pressure) and with the ARDSnet table on oxygenation and respiratory mechanics
<b>Main Results</b>	PEEP titrated by P <sub>tp</sub> was higher than by the ARDSnet table in both patients with (17.3 ±2.6 cmH <sub>2</sub> O vs. 6.3 ±1.6 cmH <sub>2</sub> O) and without IAH (9.5 ±2.1 cmH <sub>2</sub> O vs. 7.8 ±1.9 cmH <sub>2</sub> O). In patients with IAH, PaO <sub>2</sub> /FiO <sub>2</sub> was higher with PEEP titrated by P <sub>tp</sub> than by the ARDSnet table (272 ±40 mmHg vs. 209 ±50 mmHg), Crs (compliance respiratory system) and Cl (compliance of lung) were higher with PEEP titrated by P <sub>tp</sub> than by ARDSnet the table.
<b>Conclusion</b>	The use of P <sub>eso</sub> (esophageal pressure) was important in management of critically ill patients with IAH

## Comparison of 2 correction methods for absolute values of esophageal pressure in subjects with acute hypoxemic respiratory failure, mechanically ventilated in the ICU

Guérin C, Richard JC

Respir Care. 2012 Dec;57(12):2045-51

PMID 23233496, <http://www.ncbi.nlm.nih.gov/pubmed/23233496>

<b>Design</b>	Prospective interventional study
<b>Patients</b>	42 patients with ALI/ARDS
<b>Objectives</b>	Compare 2 methods for correcting absolute Pes <sub>o</sub> (esophageal pressure) value: invariant value of 5 cmH <sub>2</sub> O and the Pes <sub>o</sub> obtained at relaxation volume
<b>Main Results</b>	The end-expiratory P <sub>tp</sub> (transpulmonary pressure) corrected by 5 was 6 (1-8) cmH <sub>2</sub> O, and P <sub>tp</sub> corrected by the measured Pes <sub>o</sub> at relaxation volume was 2 (1-5) cmH <sub>2</sub> O ( $p = 0.008$ ). In 28 subjects, the end-expiratory P <sub>tp</sub> corrected by 5 was higher than P <sub>tp</sub> corrected by the measured Pes <sub>o</sub> at relaxation volume, while in 14 subjects, P <sub>tp</sub> corrected by the measured Pes <sub>o</sub> at relaxation volume was higher than P <sub>tp</sub> corrected by 5.
<b>Conclusion</b>	Correcting absolute Pes <sub>o</sub> by a value measured at relaxation volume was much accurate than an invariant value of 5 cmH <sub>2</sub> O

## ECMO criteria for influenza A (H1N1)-associated ARDS: role of transpulmonary pressure.

Grasso S, Terragni P, Birocco A, Urbino R, Del Sorbo L, Filippini C, Mascia L, Pesenti A, Zangrillo A, Gattinoni L, Ranieri VM

Intensive Care Med. 2012 Mar;38(3):395-403

PMID 22323077, <http://www.ncbi.nlm.nih.gov/pubmed/22323077>

<b>Design</b>	Prospective interventional study
<b>Patients</b>	14 patients with influenza AH1N1-associated ARDS referred for ECMO
<b>Objectives</b>	Assess whether partitioning the Ers (elastance of respiratory system) between El (elastance of lung) and Ecw (elastance of chest wall) in order to target values of end-inspiratory Ptp (transpulmonary pressure) close to its upper physiological limit (25 cmH2O) may optimize oxygenation
<b>Main Results</b>	In 7 patients, end-inspiratory Ptp was $27.2 \pm 1.2$ cmH2O; all of these patients underwent ECMO. In the other 7 patients, end-inspiratory Ptp was $16.6 \pm 2.9$ cmH2O, increasing PEEP (from $17.9 \pm 1.2$ to $22.3 \pm 1.4$ cmH2O) to approach the upper physiological limit of end-inspiratory Ptp = $25.3 \pm 1.7$ cmH2O improved oxygenation, allowing patients to be treated without ECMO. There were obese patients in both groups.
<b>Conclusion</b>	Abnormalities of chest wall mechanics may be present in some patients with influenza AH1N1-associated ARDS, so analyzing the lung and chest wall mechanics avoided ECMO.



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

Loring SH, O'Donnell CR, Behazin N, Malhotra A, Sarge T, Ritz R, Novack V, Talmor D

J Appl Physiol. 2010 Mar;108(3):515-22

PMID 20019160, <http://www.ncbi.nlm.nih.gov/pubmed/20019160>

<b>Design</b>	Parallel to EPVent physiological study
<b>Patients</b>	48 patients from EPVent
<b>Objectives</b>	Assess the credibility of Pes (esophageal pressure) by comparison with simultaneously measured gastric (Pga) and bladder pressures (Pblad)
<b>Main Results</b>	End-expiratory Pes, Pga, and Pblad averaged $18.6 \pm 4.7$ , $18.4 \pm 5.6$ , and $19.3 \pm 7.8$ cmH <sub>2</sub> O, respectively. End-expiratory Pes was correlated with Pga and Pblad and was unrelated to Ccw (compliance of chest wall). Ptp was $-2.8 \pm 4.9$ cmH <sub>2</sub> O at end expiration and $8.3 \pm 6.2$ cmH <sub>2</sub> O at end inspiration. Lung stress measured as end-inspiratory transpulmonary pressure was much less than stress inferred from the Pplat (plateau pressure), CI (compliance of lung), and Ccw by 9.6 cmH <sub>2</sub> O.
<b>Conclusion</b>	Stress calculated with $\Delta P_{tp}$ provides an incomplete measure because it avoids prestress. Pes provided meaningful information.

## Influence of lung and chest wall compliances on transmission of airway pressure to the pleural space in critically ill patients

Jardin F, Genevray B, Brun-Ney D, Bourdarias JP

Chest. 1985 Nov;88(5):653-8

PMID 3902386, <http://www.ncbi.nlm.nih.gov/pubmed/3902386>

<b>Design</b>	Prospective interventional comparative study
<b>Patients</b>	19 patients with ARF, 3 groups: Crs (compliance of respiratory system) > 45, Crs between 45 and 30, Crs < 30 ml/cmH <sub>2</sub> O
<b>Objectives</b>	Evaluate the transmission of Paw to the pleural space at end expiration and end inspiration, at three levels of PEEP
<b>Main Results</b>	In patients with Crs > 45 ml/cmH <sub>2</sub> O, 37% of Paw (airway pressure) was transmitted to the pleural space, Cl (compliance of lung) = 100.3 ± 17.2 ml/cmH <sub>2</sub> O. With Crs between 45 and 30 ml/cmH <sub>2</sub> O, 32% of Paw was transmitted to the pleural space, Cl = 45.0 ± 6.3 ml/cmH <sub>2</sub> O. With Crs < 30 ml/cmH <sub>2</sub> O, 24% of Paw (airway pressure) was transmitted to the pleural space, Cl = 28.6 ± 8.9 ml/cmH <sub>2</sub> O.
<b>Conclusion</b>	An increase in lung stiffness decreased transmission of airway pressure to the pleural space

## A simple method for assessing the validity of the esophageal balloon technique

Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J. Am Rev Respir Dis

1982 Nov;126(5):788-91

PMID 7149443, <http://www.ncbi.nlm.nih.gov/pubmed/7149443>

<b>Design</b>	Prospective interventional physiological study
<b>Patients</b>	10 subjects
<b>Objectives</b>	Determine the validity of the conventional esophageal balloon technique as a measure of pleural pressure by occluding the airways at end expiration and measuring the ratio of changes in $P_{es}$ (esophageal pressure) and mouth pressure during the ensuing spontaneous occluded inspiratory efforts
<b>Main Results</b>	$\Delta P_{es}/\Delta P_{mouth}$ values were close to unity in sitting and lateral positions. In supine positions, positioning the balloon to different levels in the esophagus allowed for finding a locus where the $\Delta P_{es}/\Delta P_{mouth}$ ratio was close to unity.
<b>Conclusion</b>	Positioning the balloon according to the "occlusion test" procedure validated measurements of pleural pressure

## Pulmonary, chest wall, and lung-thorax elastances in acute respiratory failure

Katz JA, Zinn SE, Ozanne GM, Fairley HB

Chest. 1981 Sep;80(3):304-11

PMID 6944170, <http://www.ncbi.nlm.nih.gov/pubmed/6944170>

<b>Design</b>	Prospective interventional study
<b>Patients</b>	15 patients with ARF
<b>Objectives</b>	Determine whether $E_{rs}$ (elastance of respiratory system) reflected $E_l$ (elastance of lung), $E_{cw}$ (elastance of chest wall), or both
<b>Main Results</b>	$E_{rs}$ was $27.9 \pm 2.6$ cmH <sub>2</sub> O/l, chest wall accounted for $34 \pm 2\%$ . Changes in $E_{rs}$ correlated only with changes in $E_l$ ( $r = 0.96$ ; $p < 0.001$ ) and not with $E_{cw}$ , except for 3 patients where changes in $E_{rs}$ were due to changes in $E_{cw}$ .
<b>Conclusion</b>	$P_{es}$ (esophageal pressure) measurement was important to determine whether increase in $E_{rs}$ was due to an increase in $E_l$ or $E_{cw}$

## Topography of esophageal pressure as a function of posture in man

Milic-Emili J, Mead J, Turner JM

J Appl Physiol. 1964 Mar;19:212-6

PMID 14155284, <http://www.ncbi.nlm.nih.gov/pubmed/14155284>

<b>Design</b>	Prospective interventional physiological study
<b>Patients</b>	7 healthy subjects
<b>Objectives</b>	Determine topography of esophageal pressure at various lung volumes, in various positions
<b>Main Results</b>	The upper-third pressures reflected external and mouth pressures, and changed with head posture. The lower-third pressures varied point by point and with position. The middle-third pressures were uniform.
<b>Conclusion</b>	Peso (esophageal pressure) obtained in the middle-third of esopagus more closely reflected pleural pressure

## A clinical study on mechanical ventilation PEEP setting for traumatic ARDS patients guided by esophageal pressure

Wang B, Wu B, Ran YN

Technol Health Care. 2019;27(1):37-47

PMID 30475777, <http://www.ncbi.nlm.nih.gov/pubmed/30475777>

<b>Design</b>	Randomized controlled trial
<b>Patients</b>	23 traumatic ARDS patients: 12 in esophageal pressure-guided PEEP group, 11 in ARDSnet group
<b>Objectives</b>	Explore whether PEEP guided by esophageal pressure (Pes) is better than the ARDSNet method during the treatment of traumatic ARDS patients
<b>Main Results</b>	PEEP in the Pes-guided group was higher than in the ARDSnet group ( $12 \pm 4$ cmH <sub>2</sub> O vs. $8 \pm 3$ cm H <sub>2</sub> O, $p < 0.05$ ). End-expiratory transpulmonary pressure in the Pes-guided group was $0.5 \pm 0.7$ cmH <sub>2</sub> O vs. $-1.1 \pm 3.3$ cmH <sub>2</sub> O in the ARDSnet group ( $p < 0.05$ ). In the Pes-guided group, lung compliance and the oxygenation index were higher than in the ARDSnet group. Interleukin-6 and interleukin-8 were lower in the Pes-guided group.
<b>Conclusion</b>	The use of Pes enabled identification of those traumatic ARDS patients that would benefit from higher PEEP than PEEP applied according to the ARDSnet.

## Value and limitations of transpulmonary pressure calculations during intra-abdominal hypertension

Cortes-Puentes GA, Gard KE, Adams AB, Faltesek KA, Anderson CP, Dries DJ, Marini JJ

Crit Care Med. 2013 Aug;41(8):1870-7

PMID 23863222, <http://www.ncbi.nlm.nih.gov/pubmed/23863222>

<b>Design</b>	Animal study
<b>Patients</b>	11 pigs
<b>Objectives</b>	Describe the effects of increased intra-abdominal pressure (IAP from 0 to 25 mmHg) on Peso (esophageal pressure), Ptp (transpulmonary pressure), and functional residual capacity (FRC), at two levels of PEEP (1 and 10 cmH2O)
<b>Main Results</b>	FRC was reduced by increasing IAP at both levels of PEEP, without changes of end-expiratory Peso. When IAP became higher than 5 mmHg, Pplat increased linearly by 50% of the applied IAP, with same changes in Peso. With constant Vt, negligible changes occurred in Ptp (pressure plateau). Increasing IAP reduced Ccw (compliance of chest wall), but in this case, increasing PEEP improved Ccw.
<b>Conclusion</b>	Lung collapse caused by increasing IAP was improved by increasing PEEP

## Pleural pressure and optimal positive end-expiratory pressure based on esophageal pressure versus chest wall elastance: incompatible results

Gulati G, Novero A, Loring SH, Talmor D

Crit Care Med. 2013 Aug;41(8):1951-7

PMID 23863227, <http://www.ncbi.nlm.nih.gov/pubmed/23863227>

<b>Design</b>	Retrospective study
<b>Patients</b>	64 ARDS patients managed with Peso (esophageal pressure)
<b>Objectives</b>	Compare Peso and Ecw (elastance of chest wall) for estimated pleural pressure and set PEEP
<b>Main Results</b>	Pleural pressures estimated by Peso and Ecw were different and discordant during end-expiratory occlusion and end-inspiratory occlusion. PEEP recommended by the two methods for each patient were discordant and uncorrelated.
<b>Conclusion</b>	The strategies of targeting an end-expiratory Peso-based Ptp (transpulmonary pressure) =0 cmH2O and targeting an end-inspiratory Ecw (elastance of chest wall)-based Ptp=26 cmH2O cannot be interchangeable. Ecw and Ers (elastance of respiratory system) varied unpredictably with changes in PEEP

## Volume-related and volume-independent effects of posture on esophageal and transpulmonary pressures in healthy subjects

Washko GR, O'Donnell CR, Loring SH

J Appl Physiol. 2006 Mar;100(3):753-8

PMID 16306256, <http://www.ncbi.nlm.nih.gov/pubmed/16306256>

<b>Design</b>	Prospective interventional physiological study
<b>Patients</b>	10 healthy subjects
<b>Objectives</b>	Determine the variability of postural effects on $P_{eso}$ (esophageal pressure), in relaxation volume and total lung capacity
<b>Main Results</b>	$P_{tp}$ (transpulmonary pressure) at relaxation volume averaged 3.7 (SD 2.0) cmH <sub>2</sub> O upright and -3.3 (SD 3.2) cmH <sub>2</sub> O supine. Approximately 58% of the decrease in $P_{tp}$ between the upright and supine postures was due to a corresponding decrease in relaxation volume. The remaining 2.9 cmH <sub>2</sub> O difference is consistent with reported values of a presumed postural artifact.
<b>Conclusion</b>	Adding 3 cmH <sub>2</sub> O was necessary to correct estimated $P_{tp}$ for the effect of lying supine but considering the range of $P_{tp}$ in ARF patients, the need to correct $P_{tp}$ is debatable

## Recruitment and derecruitment during acute respiratory failure: an experimental study

Pelosi P, Goldner M, McKibben A, Adams A, Eccher G, Caironi P, Losappio S, Gattinoni L, Marini JJ

Am J Respir Crit Care Med. 2001 Jul;164(1):122-30

PMID 11435250, <http://www.ncbi.nlm.nih.gov/pubmed/11435250>

<b>Design</b>	Animal study
<b>Patients</b>	6 dogs with oleic acid respiratory failure
<b>Objectives</b>	Compare pleural pressure and $P_{eso}$ (esophageal pressure) in upper nondependent, middle, and dependent lung regions
<b>Main Results</b>	There was a good Bland and Allman correlation between pleural pressure and $P_{eso}$ in nondependent, middle, and dependent regions. Significant differences were found between absolute values, but changes of pleural pressure were similar with changes of $P_{eso}$ in response to increasing $P_{aw}$ (airway pressure).
<b>Conclusion</b>	Variation in $P_{eso}$ was a reasonable estimate of variation of pleural pressure

## Validation of esophageal pressure occlusion test after paralysis

Lanteri CJ, Kano S, Sly PD

Pediatr Pulmonol. 1994 Jan;17(1):56-62

PMID 8108177, <http://www.ncbi.nlm.nih.gov/pubmed/8108177>

<b>Design</b>	Animal study
<b>Patients</b>	16 puppies
<b>Objectives</b>	Evaluate occlusion test for paralyzed subject by occluding airway and applied pressure to the abdomen or ribs and observation of positive swings in both $P_{eso}$ (esophageal pressure) and $P_{aw}$ (airway pressure)
<b>Main Results</b>	In traditional occlusion tests, $\Delta P_{eso}$ was within 10% of $\Delta P_{aw}$ . In positive pressure occlusion tests using abdominal pressure performed after paralysis, $\Delta P_{eso}$ was within 10% of $\Delta P_{aw}$ . In positive pressure occlusion tests using rib pressure, $\Delta P_{eso}$ was within 10% of $\Delta P_{aw}$ .
<b>Conclusion</b>	Accurate occlusion tests were possible in paralyzed subjects by abdominal or rib pressure during airway occlusion

## Lung mechanics in sitting and horizontal body positions

Behrakis PK, Baydur A, Jaeger MJ, Milic-Emili J

Chest. 1983 Apr;83(4):643-6

PMID 6831953, <http://www.ncbi.nlm.nih.gov/pubmed/6831953>

<b>Design</b>	Prospective interventional physiological study
<b>Patients</b>	10 healthy subjects
<b>Objectives</b>	Mesure CI (compliance of lung) in different positions
<b>Main Results</b>	CI was 210 in sitting, 190 in lateral, and 160 ml/cmH <sub>2</sub> O in supine positions. The change was significant ( $p < 0.01$ ) between the sitting and supine positions.
<b>Conclusion</b>	$P_{eso}$ (esophageal pressure) measurement was better in a sitting position. In ICU patients, the head of the bed should be greater than 45° measurement.

# Additional files

## Targeting transpulmonary pressure to prevent ventilator induced lung injury

Sarge T, Talmor D

Minerva Anesthesiol. 2009 May;75(5):293-9

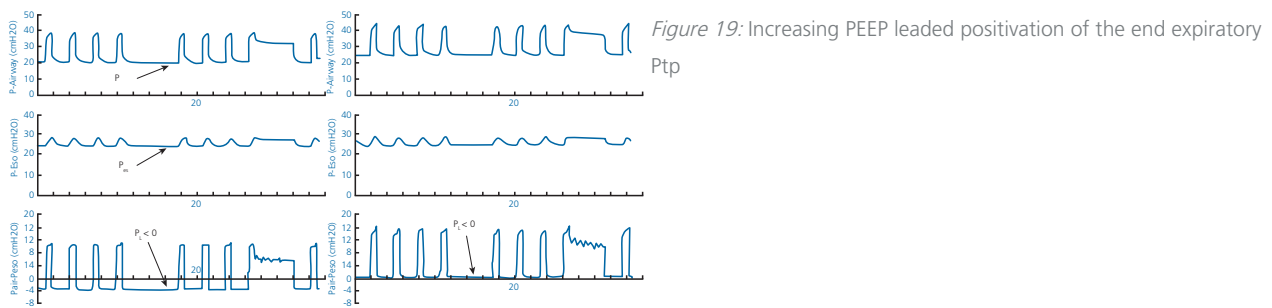
PMID 19412147, <http://www.ncbi.nlm.nih.gov/pubmed/19412147>

### Design

Review

### Conclusion

Customize the ventilator settings for ARDS patients





## Should we titrate peep based on end-expiratory transpulmonary pressure?-yes

Baedorf Kassis E, Loring SH, Talmor D

Ann Transl Med. 2018 Oct;6(19):390

PMID 30460264, <http://www.ncbi.nlm.nih.gov/pubmed/30460264>

**Design** Review

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**Conclusion** Esophageal pressure monitoring provides a window into the unique physiology of a patient and helps improve clinical decision-making at the bedside.

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## Interpretation of the transpulmonary pressure in the critically ill patient

Umbrello M, Chiumello D

Ann Transl Med. 2018 Oct;6(19):383

PMID 30460257, <http://www.ncbi.nlm.nih.gov/pubmed/30460257>

**Design** Review

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**Conclusion** Highlights the different assumptions underlying the various methods for measuring transpulmonary pressure and the potential application of transpulmonary pressure assessment during controlled and spontaneous/assisted mechanical ventilation.

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## Technical aspects of bedside respiratory monitoring of transpulmonary pressure

Mojoli F, Torriglia F, Orlando A, Bianchi I, Arisi E, Pozzi M

Ann Transl Med. 2018 Oct;6(19):377

PMID 30460251, <http://www.ncbi.nlm.nih.gov/pubmed/30460251>

**Design** Review

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**Conclusion** Describes the technique of esophageal pressure measurement: catheter insertion, proper placement and filling of the balloon, the validation test and specific procedures to remove the main artifacts.

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## Assessing breathing effort in mechanical ventilation: physiology and clinical implications

de Vries H, Jonkman A, Shi ZH, Spoelstra-de Man A, Heunks L  
Ann Transl Med. 2018 Oct;6(19):387  
PMID 30460261, <http://www.ncbi.nlm.nih.gov/pubmed/30460261>

<b>Design</b>	Review
<b>Conclusion</b>	Describes the physiological background and methodological issues of the most frequently used methods to quantify breathing effort, the work of breathing, the pressure-time product, and the level of breathing effort that may be considered optimal during mechanical ventilation at different stages of critical illness.

## Value of measuring esophageal pressure to evaluate heart-lung interactions - applications for invasive hemodynamic monitoring

Repressé X, Vieillard-Baron A, Geri G  
Ann Transl Med. 2018 Sep;6(18):351  
PMID 30370278, <http://www.ncbi.nlm.nih.gov/pubmed/30370278>

<b>Design</b>	Review
<b>Conclusion</b>	This review presents the physiological basis, the technical aspects and the value in clinical practice of the measurement of esophageal pressure to evaluate heart-lung interactions.

## Esophageal pressure monitoring: why, when and how?

Yoshida T, Brochard L

Curr Opin Crit Care. 2018 Jun;24(3):216-222

PMID 29601320, <http://www.ncbi.nlm.nih.gov/pubmed/29601320>

<b>Design</b>	Review
<b>Objectives</b>	Describe technical tips to adequately measure esophageal pressure at the bedside
<b>Main Results</b>	Each esophageal balloon has its own nonstressed volume and it should be calibrated properly. Transpulmonary pressure calculated on absolute esophageal pressure reflects values in the lung regions adjacent to the esophageal balloon (i.e., dependent to middle lung). Transpulmonary pressure calculated from lung to respiratory system elastance ratio reasonably reflects lung stress in the nondependent 'baby' lung.
<b>Conclusion</b>	There is large potential to improve clinical outcomes as an early detector of risk of lung injury from mechanical ventilation and vigorous spontaneous effort.

## Esophageal pressure: research or clinical tool?

Baedorf Kassis E, Loring SH, Talmor D

Med Klin Intensivmed Notfmed. 2018 Feb;113(Suppl 1):13-20

PMID 29134245, <http://www.ncbi.nlm.nih.gov/pubmed/29134245>

<b>Design</b>	Review
<b>Conclusion</b>	Explains the concept and clinical applications of esophageal pressure.

## Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives

Mauri T, Yoshida T, Bellani G, Goligher EC, Carteaux G, Rittayamai N, Mojoli F, Chiumello D, Piquilloud L, Grasso S, Jubran A, Laghi F, Magder S, Pesenti A, Loring S, Gattinoni L, Talmor D, Blanch L, Amato M, Chen L, Brochard L, Mancebo J; PLeUral pressure working Group (PLUG—Acute Respiratory Failure section of the European Society of Intensive Care Medicine).

Intensive Care Med. 2016 Sep;42(9):1360-73

PMID 27334266, <http://www.ncbi.nlm.nih.gov/pubmed/27334266>

<b>Design</b>	Review conducted by PLUG (PLeUral pressure working Group)
<b>Objectives</b>	Review of the relevant technical, physiological and clinical details that support the clinical utility of esophageal pressure
<b>Conclusion</b>	Esophageal pressure monitoring provides unique bedside measures for a better understanding of the pathophysiology of acute respiratory failure patients. Including esophageal pressure monitoring in the intensivist's clinical armamentarium may enhance treatment to improve clinical outcomes

## The application of esophageal pressure measurement in patients with respiratory failure

Akoumianaki E(1), Maggiore SM, Valenza F, Bellani G, Jubran A, Loring SH, Pelosi P, Talmor D, Grasso S, Chiumello D, Guérin C, Patroniti N, Ranieri VM, Gattinoni L, Nava S, Terragni PP, Pesenti A, Tobin M, Mancebo J, Brochard L.

Am J Respir Crit Care Med. 2014 Mar 1;189(5):520-31

PMID 24467647, <http://www.ncbi.nlm.nih.gov/pubmed/24467647>

<b>Design</b>	International experts conference "Plug"
<b>Patients</b>	ICU patients during passive and active ventilation
<b>Objectives</b>	Summarize current P <sub>es</sub> (esophageal pressure) knowledge and describe clinical application in mechanically ventilated patients.
<b>Main Results</b>	P <sub>es</sub> is helpful in setting P <sub>insp</sub> and PEEP in ARDS patients, in studying patient ventilator synchrony, and in understanding weaning failure
<b>Conclusion</b>	Physiological knowledge, description of the technique, clinical indications

## Driving Pressure and Transpulmonary Pressure: How Do We Guide Safe Mechanical Ventilation?

Williams EC, Motta-Ribeiro GC, Vidal Melo MF

Anesthesiology. 2019 Jul;131(1):155-163

PMID 31094753, <http://www.ncbi.nlm.nih.gov/pubmed/31094753>

**Design** Review

**Objectives** The physiological concept, pathophysiological implications, and clinical relevance and application of driving pressure and transpulmonary pressure to prevent ventilator-induced lung injury (VILI) are discussed.

**Conclusion** If there is a risk of VILI, transpulmonary pressure measurement is advisable to guide ventilatory management (as per the suggested approach)

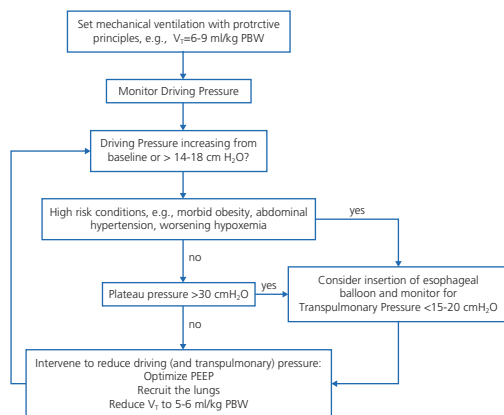


Figure 20: Approach to guide mechanical ventilation

## Targeting transpulmonary pressure to prevent ventilator-induced lung injury

Gattinoni L, Giosa L, Bonifazi M, Pasticci I, Busana M, Macri M, Romitti F, Vassalli F, Quintel M

Expert Rev Respir Med. 2019 Aug;13(8):737-746

PMID 31274034, <http://www.ncbi.nlm.nih.gov/pubmed/31274034>

**Design** Expert opinion

**Conclusion** Transpulmonary pressure represents a physiologically sound safety limit for mechanical ventilation that should be measured and targeted at least in the most severe ARDS patients.

## Transpulmonary pressure: importance and limits

Grieco DL, Chen L, Brochard L

Ann Transl Med. 2017 Jul;5(14):285

PMID 28828360, <http://www.ncbi.nlm.nih.gov/pubmed/28828360>

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**Design**

Review

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**Conclusion**

Despite limitations, assessment of transpulmonary pressure allows a deeper understanding of the risk of ventilator-induced lung injury, and may potentially help tailor ventilator settings.

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## Transpulmonary pressure: the importance of precise definitions and limiting assumptions

Loring SH, Topulos GP, Hubmayr RD

Am J Respir Crit Care Med. 2016 Dec 15;194(12):1452-57

PMID 27606837, <http://www.ncbi.nlm.nih.gov/pubmed/27606837>

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**Design**

Review

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**Conclusion**

Explains the various physiological terms to define the physical state of the lungs, the chest wall, and the integrated respiratory system, and stresses the need for consistency when using them

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## The promises and problems of transpulmonary pressure measurements in acute respiratory distress syndrome

Sahetya SK, Brower RG

Curr Opin Crit Care. 2016 Feb;22(1):7-13

PMID 26627536, <http://www.ncbi.nlm.nih.gov/pubmed/26627536>

<b>Design</b>	Review
<b>Conclusion</b>	Limitations of transpulmonary pressure measurements

## Measurement of esophageal pressure at bedside: pros and cons

Brochard L

Curr Opin Crit Care. 2014 Feb;20(1):39-46

PMID 24300619, <http://www.ncbi.nlm.nih.gov/pubmed/24300619>

<b>Design</b>	Review
<b>Conclusion</b>	Advantages and limitations of using esophageal pressure in intensive care

## Two steps forward in bedside monitoring of lung mechanics: transpulmonary pressure and lung volume

Cortese GA, Marini JJ

Crit Care 2013 March;19;17(2):219

PMID 23509867, <http://www.ncbi.nlm.nih.gov/pubmed/23509867>

<b>Design</b>	Review, Expert opinion
<b>Patients</b>	na
<b>Objectives</b>	Review the management rationale and technical background for monitoring TP pressure and FRC
<b>Main Results</b>	"It seems clear that these newly available tools, used separately and/or together, have potential to improve delivery of respiratory care by characterizing the response to interventions or to the course of disease."
<b>Conclusion</b>	Although not perfect, estimations of Ptp (transpulmonary pressure) are of more help in elucidating the interactions between patient characteristics, disease conditions, and ventilator settings than are pulmonary mechanics based on airway pressure alone

## Goal-directed mechanical ventilation: are we aiming at the right goals? A proposal for an alternative approach aiming at optimal lung compliance, guided by esophageal pressure in acute respiratory failure

Soroksky A, Esquinas A

Crit Care Res Pract. 2012;2012:597932

PMID 23019524, <http://www.ncbi.nlm.nih.gov/pubmed/23019524>

**Design** Review

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**Conclusion** Explain the use of Peso (esophageal pressure)

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## Esophageal pressure: benefit and limitations

Hedenstierna G

Minerva Anesthesiol. 2012 Aug;78(8):959-66

PMID 22699701, <http://www.ncbi.nlm.nih.gov/pubmed/22699701>

**Design** Expert Opinion

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**Conclusion** Highlights Peso (esophageal pressure) limitations

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## Esophageal and gastric pressure measurements.

Benditt JO, Proctor HJ, Woolson R.

Respir Care. 2005 Jan;50(1):68-75

PMID 15636646, <http://www.ncbi.nlm.nih.gov/pubmed/15636646>

**Design** Review

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**Patients** na

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**Objectives** Review the historical background, physiology, placement techniques, and potential clinical applications of esophageal and gastric pressure measurements.

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## Respiratory mechanics in mechanically ventilated patients

Hess DR

Respir Care. 2014 Nov;59(11):1773-94

PMID 25336536, <http://www.ncbi.nlm.nih.gov/pubmed/25336536>

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**Design**

Review

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**Conclusion**

Explains esophageal pressure measurement in ventilated patients

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