Ball *et al. Critical Care* (2024) 28:177
https://doi.org/10.1186/s13054-024-04950-y

Critical Care

REVIEW

Open Access

Transpulmonary pressure monitoring in critically ill patients: pros and cons

Lorenzo Ball[1,2*], Daniel Talmor[3] and Paolo Pelosi[1,2]

Abstract

The use of transpulmonary pressure monitoring based on measurement of esophageal pressure has contributed importantly to the personalization of mechanical ventilation based on respiratory pathophysiology in critically ill patients. However, esophageal pressure monitoring is still underused in the clinical practice. This technique allows partitioning of the respiratory mechanics between the lungs and the chest wall, provides information on lung recruitment and risk of barotrauma, and helps titrating mechanical ventilation settings in patients with respiratory failure. In assisted ventilation modes and during non-invasive respiratory support, esophageal pressure monitoring provides important information on the inspiratory effort and work of breathing. Nonetheless, several controversies persist on technical aspects, interpretation and clinical decision-making based on values derived from this monitoring technique. The aim of this review is to summarize the physiological bases of esophageal pressure monitoring, discussing the pros and cons of its clinical applications and different interpretations in critically ill patients undergoing invasive and non-invasive respiratory support.

Keywords ARDS, Transpulmonary pressure, Esophageal pressure

Introduction

Transpulmonary pressure (P_L) corresponds to the distending force (stress) applied to the lungs which results in their mechanical deformation (strain) [1]. Stress and strain are linked by a linear relationship in healthy subjects and in patients with acute respiratory distress syndrome (ARDS), namely $stress = k \bullet strain$, where k is specific elastance [2]. The correct physiological definition of transpulmonary pressure is $P_L = P_{ALV} - P_{pl}$, where P_{ALV} is the alveolar pressure and P_{pl} is the pleural pressure. While P_{ALV} equals the airway pressure (P_{AW}) under static conditions at end-inspiration or end-expiration, P_{pl} requires indirect estimation. Due to the anatomical position of the esophagus in the pleural space, esophageal pressure (P_{es}) represents a surrogate of the P_{pl} [1, 3]: therefore, in the clinical practice, transpulmonary pressure can be estimated as $P_L = P_{AW} - P_{es}$. The use of such approximation has contributed importantly to the knowledge of the respiratory pathophysiology in critically ill patients and individualization of mechanical ventilation [4]. The use of esophageal balloons to measure P_{es} requires expertise and the correct interpretation of P_{es}-derived transpulmonary pressure warrants deep understanding of the assumptions underlying the use of P_{es} as an estimate of P_{pl}. Possibly as a consequence of this complexity, esophageal pressure monitoring is still underused in the clinical practice [1] and less than 1% of patients with ARDS received this monitoring tool in a recent large international observational study [5].

The aim of this review is to summarize the physiological bases of esophageal pressure monitoring, discussing the pros and cons of its clinical applications and different

*Correspondence:
Lorenzo Ball
lorenzo.ball@unige.it
[1] Department of Surgical Sciences and Integrated Diagnostics (DISC), University of Genoa, Viale Benedetto XV 16, Genoa, Italy
[2] Anesthesia and Intensive Care, San Martino Policlinico Hospital, IRCCS for Oncology and Neurosciences, Genoa, Italy
[3] Department of Anesthesia, Critical Care, and Pain Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

interpretations in critically ill patients undergoing non-invasive and invasive respiratory support.

Determinants of esophageal pressure

In the upright position, esophageal pressure changes reflect accurately the overall changes occurring in pleural pressure applied to the lungs' surface at a specific site [6]. However, in the supine position, several factors may influence the value of pressure measured inside the esophagus using an air-filled balloon. Among them, the most important determinants of P_{es} are the following: chest wall elastance, the height of the chest wall, the distension of the abdomen pushing the diaphragm upwards and the weight of mediastinal organs lying above the esophageal balloon [7]. Moreover, the elastance of the esophageal wall, the reaction of smooth musculature to the presence of the balloon and the elastance of the esophageal balloon itself affect the measurement, while the transmission of cardiac contractions introduces artifacts which may further complicate the interpretation of P_{pl}.

Despite these known limitations, correct placement of the device allows an acceptable estimation of P_{pl} changes also in the supine position, with a good correlation with the pressure measured directly in the middle pleural space shown in experimental studies [8, 9]. Changes in body postures have been applied in a study in healthy subjects to estimate the influence of mediastinal and lung weight on P_{es}, which resulted in a mean of 3 cmH_2O [10]. If not accounted for, this additional pressure results in slight overestimation of the P_{pl}, thus underestimation of the P_L, in the dependent lung regions and in slight underestimation of the P_{pl}, thus overestimation of the P_L, in the most non-dependent lung regions. Moreover, esophageal balloons are often placed in patients requiring enteral feeding, however, the presence of a nasogastric tube does not alter significantly the measurement of P_{es} [11], and the industry has made available catheters combining the function of a nasogastric tube and an esophageal pressure probe [12].

Use of P_{es} as a surrogate for P_{pl}

Pros: The absolute value of P_{es} represents a reasonable surrogate of the P_{pl} and allows a pragmatic estimation of transpulmonary pressure at the bedside.

Cons: The P_{es} can become different from the actual P_{pl} in case of relevant weight of the mediastinum and injured lungs, which can be difficult to assess at the bedside.

Esophageal balloon positioning

The pressure inside the esophagus varies along its axis. Pressure is irregular in different portions of the esophagus as assessed using multi-probe high resolution manometry [13]. Nonetheless, all studies in respiratory physiology focused on measurements performed in the distal third of the esophagus: correct placement of the probe is therefore crucial. However, a study comparing middle (20–35 cm from the mouth) versus distal (40–45 cm from the mouth) esophageal probe positioning showed minimal influence on estimates of P_L [14], suggesting that a certain margin of flexibility can be accepted. The presence of cardiac pulse artifacts further confirms the positioning in the lower esophageal third. Certain manufacturers of esophageal balloons inserted a radio-opaque marker to allow radiological confirmation of the correct positioning [12]. In addition to correct positioning, adequate inflation volume of the probe is key to correct interpretation of esophageal pressure.

Use of standard positioning based on insertion depth

Pros: Adequate in most patients.

Cons: In case of extremely short or tall patients positioning adjustments may be necessary, as is the case of subjects with anatomical variants resulting in difficult insertion. Moreover, blind positioning may cause accidental misplacement in the airway in deeply sedated patients; in this case, direct or video-laryngoscopy should be considered to confirm correct positioning.

Esophageal balloon inflation

Most esophageal probes manufacturers suggest inflating the balloon with a fixed amount of air, in a range from 0.5 to 4 ml, according to the size and elastic properties of the device. However, technical characteristics of the balloon such as diameter, size, material and compliance of the cuff affect the transmission of pressure changes in the chest wall to the balloon according to its inflation volume [15]. Several authors suggest titrating volume inflation individually. In fact, under-filling would result in minimal cardiac artefacts [16] but under-estimation of both baseline P_{es} and P_{es} swings during tidal breathing, while over-filling would over-estimate P_{es} [17]. An optimal inflation should be aimed at maintaining the ratio of changes of the P_{es} and P_{aw} closest to 1 during an airway occlusion test [18], while other experts suggested inflating it in order to remain in the linear part of the esophageal balloon pressure–volume curve while maximizing the difference between $P_{es,end\text{-}inspiratory}$ and $P_{es,end\text{-}expiratory}$ [15]. Since most balloons are connected to the ventilator auxiliary port or dedicated monitoring system through a three-way stopcock and a tube, air leaks may occur: balloon filling should be checked periodically to ensure quality of measurements. To reduce transmission of cardiac noise and to minimize the risk of leaks, liquid-filling

of balloons has been proposed [19], but seldom used in the clinical practice.

Use of standard balloon inflation volume

Pros: Inflating the balloon based on the manufacturer recommendations provides acceptable measurements of P_{es} in many clinical conditions.

Cons: Standard inflation volume can result in over- or under-estimation of P_{pl} and individual titration could be necessary to avoid misinterpretation of P_L.

Occlusion maneuvers to confirm positioning and inflation

As discussed above, positioning and inflation of the balloon both influence the P_{es}. Correct positioning and filling can be checked using an occlusion test: when the airway is occluded at end-expiration, changes in P_{pl} are transmitted to the airway through the lungs. During occlusion, the changes of P_{es} (ΔP_{es}) equal the changes of the P_{aw} (ΔP_{aw}), thus their ratio should be 1 ($\Delta P_{es}/\Delta P_{aw} = 1$) [18], assuming that $P_{pl} = P_{es}$. A tolerance of 10% or 20% is normally considered acceptable, corresponding to $\Delta P_{es}/\Delta P_{aw}$ from 0.9 to 1.1 or from 0.8 to 1.2, respectively. In spontaneously breathing patients, airway pressure changes assessed during the occlusion test correspond to the negative P_{es} swings due to the isometric inspiratory efforts (Fig. 1). In sedated passive patients, pressure changes must be induced with gentle external chest compressions (Fig. 2), sufficient to generate a safe but measurable ΔP_{aw}, typically values between 5 and 15 cmH_2O are aimed for. When ΔP_{aw} and ΔP_{es} are equal, their difference, namely the ΔP_L, is zero. In modern ventilators and monitors able to plot the P_L tracing in real-time (green plots in Figs. 1 and 2), verifying that P_L remains constant during inspiratory efforts or chest compressions at the occlusion test further confirms the correct positioning and inflation of the balloon. Figures 1 and 2 illustrate these concepts and propose an algorithm for assessment of balloon positioning and filling. It must be stressed that aiming for a specific range of acceptability of the ratio between when ΔP_{es} and ΔP_{aw} corresponds mathematically to the introduction of a systematic percent error of 10 to 20%. This has important implications especially in patients in which the calibration was performed with small changes in the ΔP_{es}, namely those that are spontaneously breathing with a limited inspiratory effort or those in controlled ventilation in which chest compressions resulted in small changes of the ΔP_{es}. In these subjects, while during the calibration the absolute differences between ΔP_{es} and ΔP_{aw} are limited, a 10–20% percent error may result in large absolute errors when high inspiratory pressures or elevated inspiratory efforts are generated during tidal breathing.

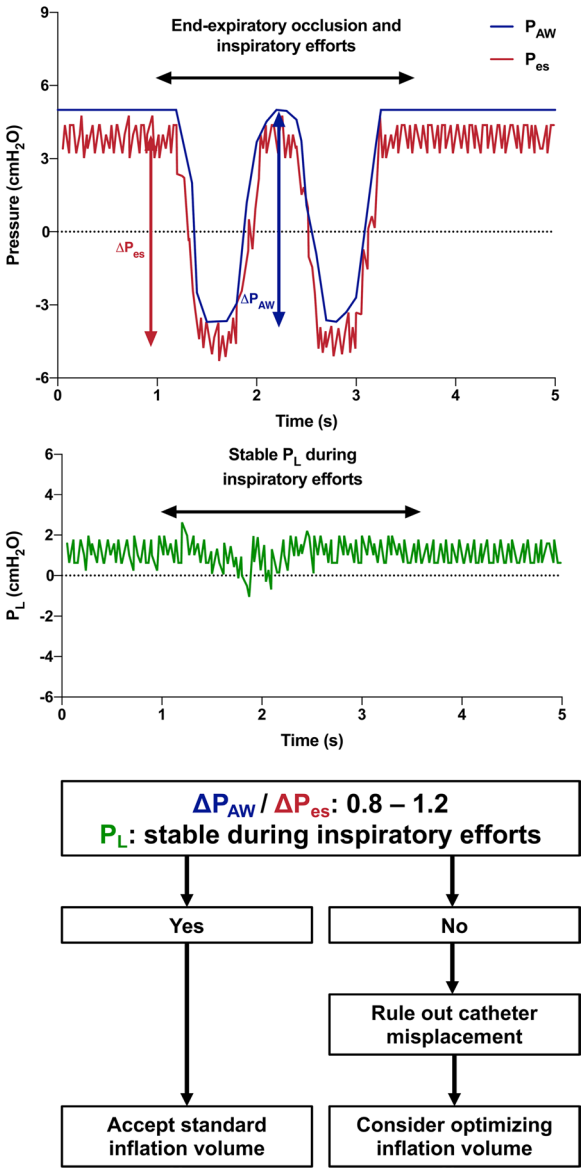


Fig. 1 Occlusion test to confirm correct positioning and inflation of the esophageal balloon in an active patient receiving assisted ventilation. An end-expiratory occlusion is performed, during which negative deflections of the pleural (P_{es}) and airway (P_{AW}) pressures are observed. During inspiratory efforts, the transpulmonary pressure (P_L) remains stable

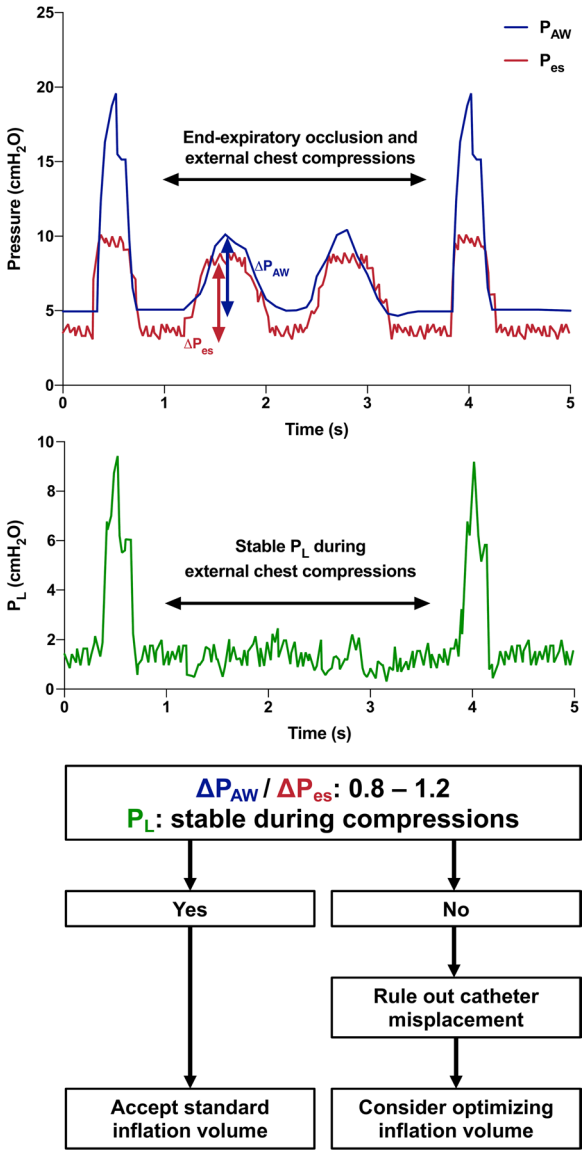


Fig. 2 Occlusion test to confirm correct positioning and inflation of the esophageal balloon in a sedated patient without spontaneous breathing activity receiving controlled ventilation. An end-expiratory occlusion is performed, and gentle external chest compressions are delivered. Positive swings of the pleural (P_{es}) and airway (P_{AW}) pressures reflect the increase in intrathoracic pressure due to the external compressions. During the occlusion maneuver, the transpulmonary pressure (P_L) remains stable

Occlusion test and external chest compression test to verify inflation and positioning

Pros: Simple and established method for verifying positioning and inflation of the balloon.

Cons: Balloon misplacement could be difficult to assess especially in passive conditions, where the magnitude of balloon pressure swings could suggest correct positioning also when the balloon is not in the distal third of the esophagus. In active patients, inspiratory efforts may be irregular, making titration of balloon inflation difficult.

Interpretation of esophageal pressure in controlled ventilation

Once ensured the correct positioning and inflation of the esophageal balloon, further reasoning and computations are necessary to use it as a tool to titrate mechanical ventilation settings.

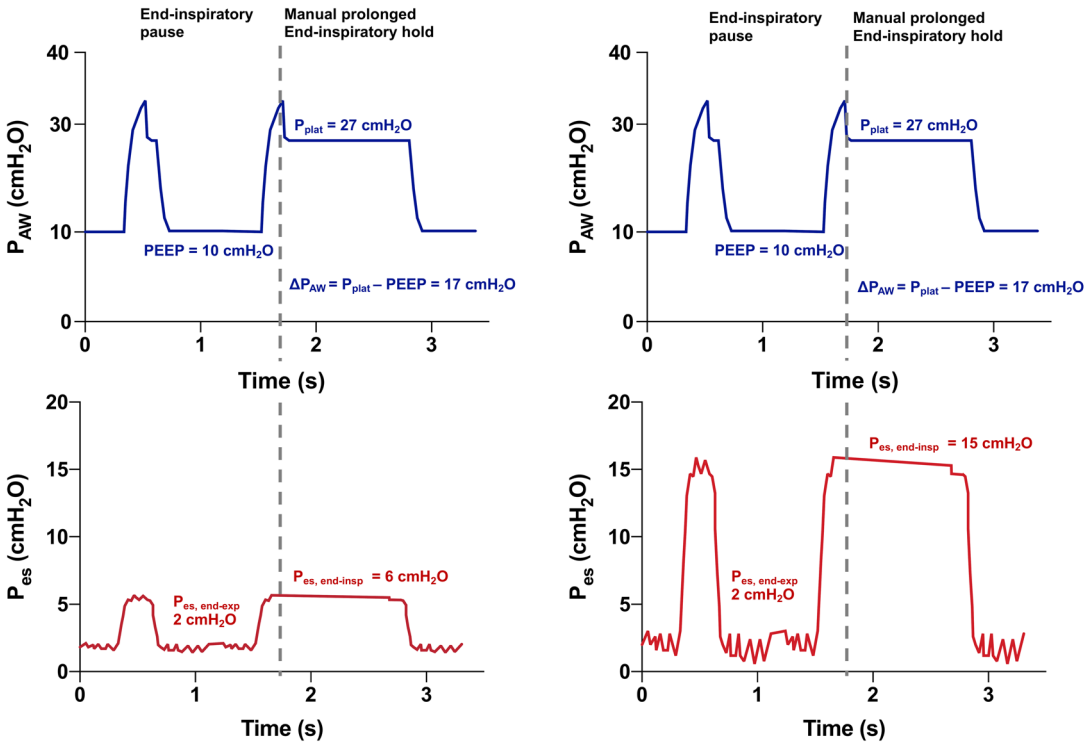
Absolute values and partitioning of respiratory mechanics

The simplest application of esophageal pressure monitoring in passive mechanically ventilated patients is the partitioning of the respiratory system elastance (E_{rs}) in its two components: lung elastance (E_L) and chest wall elastance (E_{cw}) [1, 3, 20]. Elastance is defined as the ratio between pressure changes and volume changes, is measured in cmH_2O/L and is the reciprocal of compliance (C), thus $E = 1/C$. Elastance has additive properties, therefore $E_{rs} = E_L + E_{cw}$ and since volume changes of the lungs are reflected by equal volume changes of the chest wall due to their anatomical contiguity, such property translates to the driving pressure (ΔP), namely the difference between end-inspiratory and end-expiratory pressure during tidal breathing. Therefore $\Delta P_{rs} = \Delta P_L + \Delta P_{cw}$, where ΔP_{cw} equals the driving esophageal pressure (ΔP_{es}). As illustrated in Fig. 3, at equal plateau pressures measured at the ventilator, a patient with increased E_{cw} will have lower end-inspiratory transpulmonary pressure and correspondingly a lower lung strain. This is the pathophysiological basis of the concept that higher airway plateau pressures could be tolerated in case of increased E_{cw}, such as in obese patients [21] or those with intraabdominal hypertension [22].

Partitioning of lung and chest wall elastance based on esophageal pressure

Pros: Esophageal pressure monitoring allows partitioning of total respiratory system mechanics in its pulmonary and chest wall components.

Cons: There is limited consensus on safe upper limits of end-inspiratory and tidal driving transpulmonary pressures. End-inspiratory transpulmonary pressures below 15–20 cmH_2O and tidal driving pressures below 10–12 cmH_2O may be acceptable in



$P_{L,\,end\text{-}exp} = PEEP - P_{es,\,end\text{-}exp} = 10 - 2 = 8\ cmH_2O$

$P_{L,\,end\text{-}insp} = P_{plat} - P_{es,\,end\text{-}insp} = 27 - 6 = 21\ cmH_2O$

$\Delta P_L = P_{L,\,end\text{-}insp} - P_{L,\,end\text{-}exp} = 21 - 8 = 13\ cmH_2O$

$\Delta P_{CW} = \Delta P_{ES} = P_{es,\,end\text{-}insp} - P_{es,\,end\text{-}exp} = 6 - 2 = 4\ cmH_2O$

$$\frac{E_L}{E_{TOT}} = \frac{\Delta P_L}{VT} \Big/ \frac{\Delta P_{AW}}{VT} = \frac{\Delta P_L}{\Delta P_{AW}} = \frac{13}{17} = 0.76$$

$P_{L,\,end\text{-}exp} = PEEP - P_{es,\,end\text{-}exp} = 10 - 2 = 8\ cmH_2O$

$P_{L,\,end\text{-}insp} = P_{plat} - P_{es,\,end\text{-}insp} = 27 - 15 = 12\ cmH_2O$

$\Delta P_L = P_{L,\,end\text{-}insp} - P_{L,\,end\text{-}exp} = 12 - 8 = 4\ cmH_2O$

$\Delta P_{CW} = \Delta P_{ES} = P_{es,\,end\text{-}insp} - P_{es,\,end\text{-}exp} = 15 - 2 = 13\ cmH_2O$

$$\frac{E_L}{E_{TOT}} = \frac{\Delta P_L}{VT} \Big/ \frac{\Delta P_{AW}}{VT} = \frac{\Delta P_L}{\Delta P_{AW}} = \frac{4}{17} = 0.24$$

Fig. 3 Airway pressure (top panels) and esophageal pressure (lower panels) of a patient with normal (left) or increased (right) chest wall elastance. At the same increased airway plateau and driving pressures (27 and 17 cmH_2O, respectively), the resulting transpulmonary pressure at end-inspiration and the transpulmonary driving pressure is lower in the patient with increased chest wall elastance. The elastance ratio is reported, showing that in the left patient 76% of the total elastance is constituted by lung elastance, while only 24% in the patient on the right. P_{AW}: airway pressure; P_{es}: esophageal pressure; P_{CW}: pressure of the chest wall; P_L: transpulmonary pressure; P_{plat}: plateau pressure; PEEP: positive end-expiratory pressure

ARDS. Conventional partitioning does not account for regional differences in pleural pressure.

Elastance-derived interpretation

The elastance-derived method proposes to use the ratio of the lung elastance to the total elastance (elastance ratio, E_L/E_{rs}) as a multiplicative correction factor to apply to pressures measured at the ventilator (Fig. 3) [23]. The E_L/E_{rs} ratio can be measured as $(\Delta P_{rs} - \Delta P_{es})/\Delta P_{rs}$ under passive conditions, and typically ranges from 0.5 or lower to 0.9 in critically ill patients with ARDS. It can be seen as the fraction of the airway pressure that is transmitted to the lungs. According to this method, inspiratory transpulmonary pressure is corrected as $P_{plat,elastance\text{-}derived} = P_{plat} \times E_L/E_{rs}$ and has been shown to reflect accurately the regional transpulmonary pressure in the non-dependent regions [9]. This method has been extensively used by some research groups [24]; however, when used as guidance to set positive end-expiratory pressure (PEEP) it has poor agreement with methods relying on the absolute values of P_{es} [25].

Elastance-derived interpretation of transpulmonary pressure

Pros: The elastance-derived interpretation of transpulmonary pressure provides an estimate of how the inspiratory pressure is partitioned between lung and chest wall in passive patients.

Cons: This method tends to reflect the elastic properties of the ventral lung, with limited information on the dependent dorsal regions.

PEEP-release method

To avoid the possible confounding factor of PEEP on the elastic properties of the chest wall, the PEEP-release method was proposed, based on the comparison of the transpulmonary pressure values during tidal breathing at PEEP with those obtained at zero end-expiratory pressure [2, 26]. Details on this calculation are provided in Fig. 4; as for the elastance-derived method, there is poor agreement between the values obtained with this method and those relying on absolute values of P_{es}.

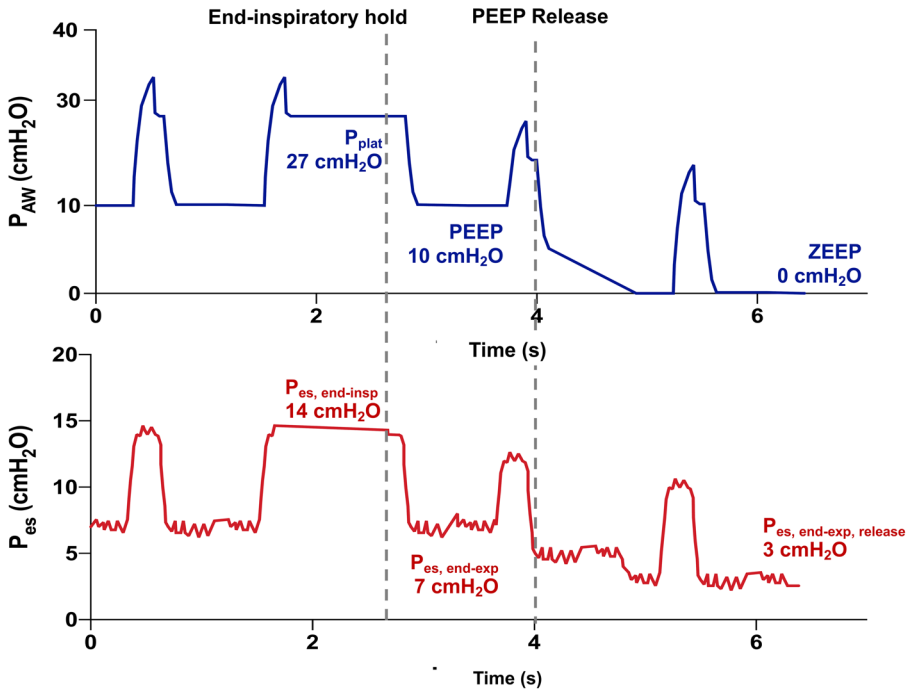
PEEP-release interpretation of transpulmonary pressure

Pros: This method could allow measuring transpulmonary pressure avoiding the effect of PEEP on the chest wall.

Cons: This method is complex, has limited acceptance and requires acquiring respiratory mechanics data at PEEP of 0 cmH_2O, a procedure raising safety concerns in severely hypoxemic patients.

PEEP-step method

A research group proposed a method to estimate the transpulmonary pressure without an esophageal balloon, based on the measurement of the end-expiratory lung volume changes following an abrupt change in PEEP [27]. This method has been validated in an in-vitro model [28], but assumes implicitly that the end-expiratory



Absolute Values

$P_{L, end-exp} = PEEP - P_{es, end-exp} = 10 - 7 = 3\ cmH_2O$

$P_{L, end-insp} = P_{plat} - P_{es, end-insp} = 27 - 14 = 13\ cmH_2O$

PEEP-release Method

$P_{L, end-exp} = (PEEP - ZEEP) - (P_{es, end-exp} - P_{es, end-exp,release}) = (10-0) - (7-3) = 6\ cmH_2O$

$P_{L, end-insp} = (P_{plat} - ZEEP) - (P_{es, end-insp} - P_{es, end-exp,release}) = (27-0) - (14-3) = 16\ cmH_2O$

Fig. 4 Comparison between transpulmonary pressure computed based on absolute values and using the PEEP-release method. From an initial PEEP of 10 cmH_2O a peep-release maneuver is performed to measure the value of the end-expiratory esophageal pressure at ZEEP. P_{AW}: airway pressure; P_{es}: esophageal pressure; P_L: transpulmonary pressure; P_{plat}: plateau pressure; PEEP: positive end-expiratory pressure; ZEEP: zero end-expiratory pressure

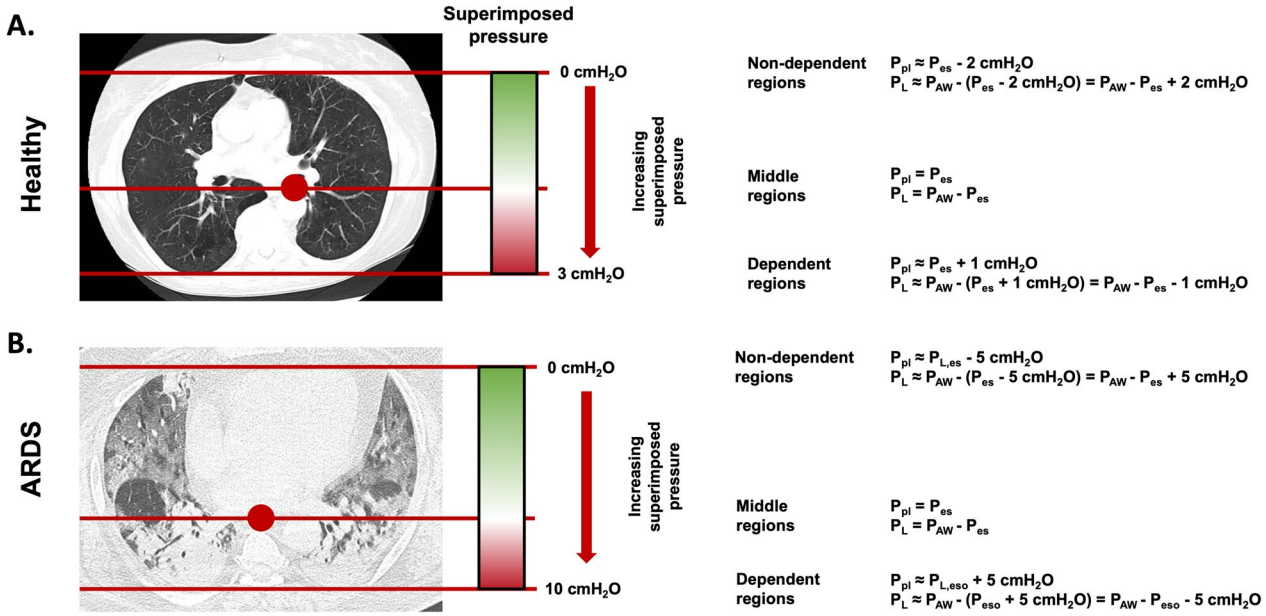


Fig. 5 Contribution of the superimposed pressure to the esophageal pressure in a healthy patient (**A**) and in one with ARDS (**B**). Esophageal pressure under-estimates the transpulmonary pressure in non-dependent regions while over-estimates that in the dorsal ones, especially in injured lungs. P_{AW}: airway pressure; P_{es}: esophageal pressure; P_L: transpulmonary pressure; P_{plat}: plateau pressure

transpulmonary pressure estimated with esophageal manometry is zero regardless of the applied PEEP level, which is contradicted by other clinical studies [29, 30].

PEEP-step method estimation of transpulmonary pressure

Pros: This method could allow estimating transpulmonary pressure without an esophageal balloon.

Cons: Limited validation and clinical acceptance.

Regional variability of pleural pressure and application of correction factors

An important determinant of the P_{pl} at the regional level is the presence of the hydrostatic pressure due to the weight of lung tissue and mediastinum lying above the level at which P_{pl} is measured [31, 32]. This results in a ventral to dorsal gradient of the P_{pl} in the supine position; as a consequence, P_{es} approximates accurately the P_{pl} only measured at the level corresponding to the position of the esophagus in the chest wall [9]. As illustrated in Fig. 5A, in healthy lungs the superimposed pressure in the most dorsal regions is around 3 cmH_2O [33], therefore assuming that the esophagus lies in an intermediate position in the ventral-dorsal axis, the P_{pl} in the most ventral or dorsal regions could deviate from the measured P_{es} by ± 1.5 cmH_2O, a negligible value in most clinical settings. In ARDS, the weight of the injured lungs increases this gradient when fully supine to an average value of 10 cmH_2O [31] (Fig. 5B), therefore $P_{pl,\ dorsal} \approx P_{es} + 5$ cmH_2O and $P_{pl,ventral} \approx P_{es} - 5$ cmH_2O [9]. The superimposed pressure in ARDS is therefore in the same order of magnitude of pressure changes applied to titrate mechanical ventilation at the bedside, notably PEEP. This has practical consequences when using P_{es} to guide clinical decisions. In fact, titrating mechanical ventilation parameters including PEEP using the P_{es} as estimate of the average P_L is equivalent to targeting the middle regions of the lungs. This may lead to airway pressures insufficient to fully recruit dorsal regions, but still resulting in hyperdistension in ventral regions.

Use of correction factors on P_{es} to estimate regional P_{pl}

Pros: The application of correction factors of ± 5 cmH_2O may provide an estimate of regional P_{pl} in ARDS, to allow separate assessment of P_L in lung regions at risk of de-recruitment versus those at risk of barotrauma.

Cons: Correction factors complicate substantially the interpretation of P_{es}. Titrating ventilation settings based on the uncorrected value of P_{es} already represents a compromise between the risk of dorsal lung de-recruitment and ventral hyper-distension.

PEEP titration based on end-expiratory transpulmonary pressure

The absolute end-expiratory transpulmonary pressure, when P_{es} is assumed equal to P_{pl}, is

$P_{L,end\text{-}exp} = PEEP_{tot} - P_{es,end\text{-}exp}$. Its value in patients with ARDS typically ranges between −10 to +10 cmH_2O and is influenced by PEEP [34] and positioning [35]. Negative values of $P_{L,end\text{-}exp}$ are associated with de-recruitment in dependent lung regions, as confirmed in studies based on electrical impedance tomography (EIT) [36]. A first randomized trial comparing a PEEP titration strategy aimed at maintaining strictly non-negative $P_{L,end\text{-}exp}$ showed improvement of oxygenation compared to a conventional low-PEEP/FiO_2 table strategy [30]. However, this strategy was not superior to the conventional high-PEEP/FiO_2 table in a larger randomized trial [37]. Nonetheless, a sub-study of the latter trial identified that titration of PEEP to $P_{L,end\text{-}exp}$ to near-zero values (±2 cmH_2O) was associated with improved mortality, whereas higher values could result in high static strain and higher mortality [38].

PEEP titration based on end-expiratory transpulmonary pressure

Pros: This approach may help identifying patients with relevant amount of de-recruited lung tissue and to individualize PEEP setting.

Cons: Randomized trials did not show clear mortality benefits. Increasing PEEP to excessively positive $P_{L,end\text{-}exp}$ could be associated with worse outcome.

Use of transpulmonary pressure to assess the risk of VILI

Exposure of lung regions to excessively elevated inspiratory pressures is a major determinant of ventilator-induced lung injury (VILI) [39]. This risk is higher in non-dependent ventral regions that receive most ventilation in ARDS in the supine position during controlled ventilation in passive patients. At end-inspiration, the P_L in the ventral lung is correctly estimated by the elastance-derived method or applying a correction of +5 cmH_2O on the absolute measurement of P_L [9]; however, also the application of a fixed correction factor is simplistic, as its exact value depends on the severity of ARDS. To assess dynamic strain, the transpulmonary driving pressure (ΔP_L) could be used, computed as $P_{L,end\text{-}insp}$ minus $P_{L,end\text{-}exp}$.

Assessment of risk of VILI using transpulmonary pressure

Pros: Limiting inspiratory and driving transpulmonary pressure could protect the lungs from excessive stress and strain. The elastance-derived method or the application of a correction factor of +5 cmH_2O on absolute measurements reflects the stress applied to the ventral regions.

Cons: Lack of consensus on safety thresholds.

Interpretation of esophageal pressure in assisted ventilation

The applications of esophageal pressure monitoring in actively breathing patients receiving invasive assisted ventilation require separate considerations. The activation of inspiratory muscles generates a negative deflection of the P_{pl}, the magnitude of this deflection is referred to as ΔP_{es} (Fig. 6). This negative pressure is maintained for a certain amount of time, that is the neural inspiratory time, and initially is spent to activate the ventilator's inspiratory trigger and to overcome intrinsic (auto) PEEP and inspiratory resistive forces, then it is released to allow end of inspiration and cycling. The pressure generated by inspiratory muscles is defined as $P_{mus} = P_{CW,recoil} - P_{es}$, where $P_{cw,recoil}$ represents the pressure that would have been generated in the chest wall by the same gas volume in absence of inspiratory effort (Fig. 6, blue line). The maximum inspiratory transpulmonary pressure is the difference between the inspiratory airway pressure and the minimum P_{es} during the inspiratory effort (Fig. 6, green arrow). In case of increased inspiratory drive, very high P_L values could be reached when a highly negative P_{es} is added to the ventilator's inspiratory pressure.

Assessment of inspiratory effort and work of breathing

When titrating respiratory support in assisted ventilation modes, clinicians should ideally target the work of breathing (WOB): low WOB may reflect over-assistance or over-sedation, while higher WOB may indicate under-assistance or excessive respiratory effort and risk of patient self-inflicted lung injury [40]. Nonetheless, computation of WOB is complex, as it is defined as the area of the inspiratory portion of the inspiratory muscle pressure (P_{mus})—volume loop [3]. From a mathematical standpoint, this corresponds for each breath to:

$$WOB_{breath} = \int_{T_{insp}} P_{mus} dV$$

The WOB can be then expressed in Joules per liter of generated volume ($WOB_{volume} = WOB_{breath}/V_T$) or per minute of ventilation ($WOB_{minute} = WOB_{breath} \bullet RR$) [41]. A limitation of this definition of WOB is that any inspiratory effort not generating a tidal volume will be zero, leading to a misinterpretation of the role of ineffective inspiratory efforts and other asynchronies. Moreover, integration over a volume is a complex computation, therefore a surrogate based on integration over time is often used: the esophageal pressure–time product ($PTP_{es} = \int_{T_{insp}} P_{mus} dt$, see Fig. 6). The PTP_{es} has been suggested to have a target range of 50 to 150 $cmH_2O \cdot s$ [3] and can be calculated also for ineffective efforts. Still, computation of $P_{cw,recoil}$ to obtain the P_{mus} requires

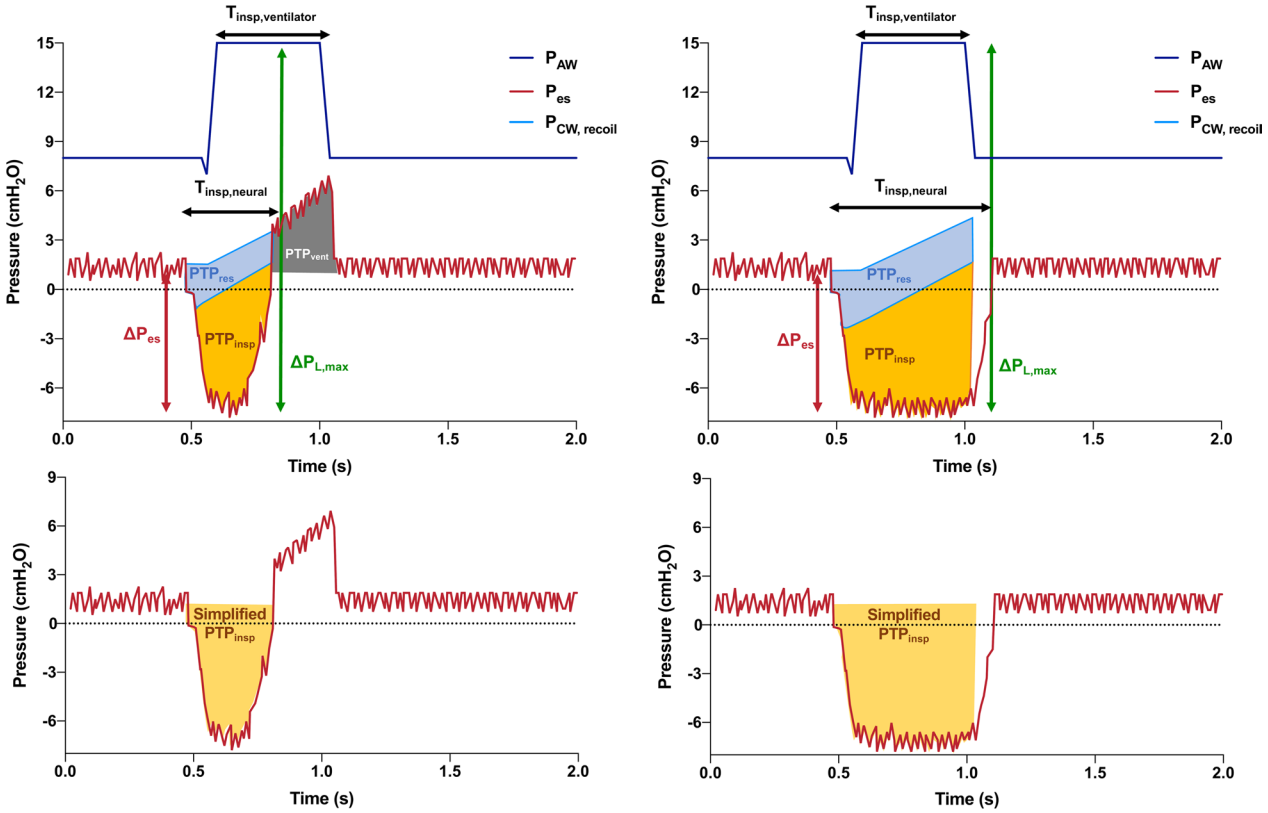


Fig. 6 Computation of the pressure–time product (PTP) in two patients with equal magnitude of esophageal pressure swings (ΔP_{es}) but short (left) versus prolonged (right) neural inspiratory time. When the inspiratory effort is initiated, the patient has first to overcome the intrinsic PEEP (PTP_{res}, blue area, top panels), then the negative pressure is maintained for the duration of the neural inspiratory time (PTP_{insp}, yellow regions, top panels). The patient on the right, compared to that on the left, has an higher PTP at the same ΔP_{es}. If the inspiratory effort is terminated before the end of the ventilator inspiratory time, the patient acts as a passive patient in the late phase of inspiration, when the esophageal pressure increases because of the ventilator inspiratory pressure (PTP_{vent}). The slope of the recoil pressure is chest wall elastance; when this is not known, PTP can be approximated integrating the P_{es} instead of the P_{musc} (simplified PTP_{insp}, lower panels). P_{AW}: airway pressure; P_{es}: esophageal pressure; P_L: transpulmonary pressure; $P_{CW,recoil}$: pressure of the chest wall under passive conditions; PEEP: positive end-expiratory pressure

knowing the E_{CW} (slope of the blue line in Fig. 6), which cannot be easily measured in active patients. Even if E_{CW} is measured in the same patient under passive conditions before initiation of assisted ventilation, it is unknown how E_{CW} varies when sedation is reduced, or neuromuscular blockade withheld to allow spontaneous breathing. Most experimental studies computed the $P_{cw,recoil}$ based on either the predicted value of E_{CW} or assuming a fixed value of 5 cmH_2O/L. The PTP_{es} and WOB are correlated and provide a precise quantification of the strength of inspiratory muscle activity, and PTP is well correlated to the metabolic cost of breathing, namely oxygen consumption [42]. The use of E_{CW} to account for the role of chest wall in inspiratory effort implies that the lung total volume is above the threshold point of the pressure–volume loop where the chest wall is in relaxation conditions [43]: this may not be the case in patients with respiratory failure with reduced total lung volume, thus questioning the routine use of the $P_{cw,recoil}$ to measure the PTP in patients with ARDS. Thus, a further simplification consists in ignoring the $P_{cw,recoil}$ when computing the PTP_{es} (simplified PTP_{es}, bottom panels in Fig. 6). Both the conventional and the simplified PTP are computed after off-line post-processing of respiratory tracings in the context of clinical research, with little to no application in the current clinical practice. The only measure that can be obtained in real-time at the bedside is the magnitude of esophageal pressure swings (ΔP_{es}), which is a rough estimate of inspiratory effort. However, this could reflect inaccurately the WOB: the same ΔP_{es} will result in different PTP_{es} if applied for a short versus long neural inspiratory time (Fig. 6, left and right panels).

Esophageal pressure monitoring represents the reference method to measure of inspiratory muscle activity and driving transpulmonary inspiratory pressure. Due to its complexity, several alternative methods based on ventilator measurements not requiring the insertion of an esophageal balloon have been proposed to guide the level

of respiratory assistance and weaning from mechanical ventilation. These include the airway occlusion pressure at 100 ms from onset of inspiration (P_{01}) [44], end-inspiratory occlusion [45] and brief end-expiratory occlusion [46] tests.

Quantification of inspiratory activity based on transpulmonary pressure in active patients

Pros: Monitoring P_{es} during assisted spontaneous breathing allows estimation of inspiratory muscles activity.

Cons: Except for ΔP_{es}, measurements are complex. In several clinical scenarios, surrogates not requiring esophageal pressure monitoring could be used to identify patients with excessively high inspiratory activity.

Assessment of maximum inspiratory transpulmonary pressure

Most research on transpulmonary pressure monitoring in assisted ventilation focused on the quantification of respiratory effort. However, high inspiratory transpulmonary pressures can be achieved also during assisted breathing [40, 47]. Figure 6 illustrates two patients receiving assisted ventilation highlighting the maximum P_L achieved during a respiratory cycle; since the end-expiratory P_L can be different from 0, this does not necessarily correspond to the sum of ΔP_{es} and ΔP_{aw} (Fig. 6, top panels). Also without esophageal pressure monitoring, an end-inspiratory occlusion performed in a cooperative patient under relaxation conditions could provide an indirect estimate of the maximum inspiratory P_L during tidal breathing [45].

Monitoring inspiratory transpulmonary pressure in active patients

Pros: Limiting inspiratory transpulmonary pressure could protect the lungs during assisted breathing.

Cons: Lack of established thresholds of safe P_L during assisted spontaneous breathing.

Assessment of asynchronies

Unintended interactions between the patient respiratory muscle activity and the ventilator are referred to as patient-ventilator asynchronies and are associated with worse clinical outcomes in critically ill patients [48], even though a causal link between asynchronies and mortality has not been established. Esophageal pressure monitoring allows precise identification of the matching between patient efforts and respiratory acts delivered by the ventilator. While P_{es} can be considered a reference method for detection of asynchronies, visual inspection of ventilator curves by experienced clinicians identifies correctly most asynchronies [49].

Monitoring of asynchronies using esophageal pressure in active patients

Pros: Allows precise monitoring of all types of patient-ventilator asynchronies.

Cons: In most cases, asynchronies can be detected by visual inspection of flow-time and airway pressure–time curves on the ventilator.

Applications during non-invasive respiratory support

The same considerations discussed in active patients also apply to those receiving non-invasive respiratory support such as conventional or high-flow oxygen therapy, continuous positive airway pressure (CPAP) and bilevel non-invasive ventilation (NIV). In these circumstances, high inspiratory drive may be associated with increased risk of barotrauma [40] and need for endotracheal intubation [50, 51]. Nonetheless, assessing inspiratory effort in these patients is particularly difficult. In patients receiving oxygen therapy few parameters in addition to clinical examination can give rough estimates of the inspiratory effort, including respiratory rate, level of dyspnea, diaphragm ultrasound and nasal pressure swings [52, 53]. In patients receiving positive-pressure respiratory support through a ventilator and non-invasive interfaces such as masks or helmets, occlusion-derived maneuvers on the ventilator typically give unreliable information on the inspiratory effort due to the confounding effect of the interface volume and compliance [54]. Monitoring P_{es} provides unique information in this setting, but this remains a largely underexplored field as clinicians tend to be reluctant in inserting an esophageal balloon in an awake hypoxemic patient [55].

Monitoring transpulmonary pressure during non-invasive respiratory support

Pros: Measurement of inspiratory effort in a challenging clinical scenario where few alternatives are available.

Cons: Requires placement of an esophageal balloon in an awake, hypoxemic patient with related discomfort and potential risks.

Conclusions

Transpulmonary pressure monitoring based on measurement of esophageal pressure substantially improved our knowledge of the pathophysiology and management of critically ill patients with respiratory failure. However, the physiology behind its interpretation is complex, and simplistic approaches have so far failed in enlarging the number of clinicians routinely using this technique. The

availability of modern esophageal probes, ventilators and dedicated monitors makes this technique applicable in any modern intensive care unit. Despite the availability of alternative methods, the use of esophageal pressure monitoring should be encouraged in the clinical practice as it improves understanding of respiratory failure and personalization of mechanical ventilation in critically ill patients.

Acknowledgements
This paper is dedicated to the family of Professor Paolo Pelosi.

Author contributions
All authors contributed equally to this manuscript.

Funding
Institutional funding only.

Availability of data and materials
Not applicable.

Code availability
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 28 March 2024 Accepted: 10 May 2024
Published online: 25 May 2024

References

1. Akoumianaki E, Maggiore SM, Valenza F, Bellani G, Jubran A, Loring SH, et al. The application of esophageal pressure measurement in patients with respiratory failure. Am J Respir Crit Care Med. 2014;189:520–31.
2. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, et al. Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med. 2008;178:346–55.
3. Mauri T, Yoshida T, Bellani G, Goligher EC, Carteaux G, Rittayamai N, et al. Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. Intensive Care Med. 2016;42:1360–73.
4. Pelosi P, Ball L, Barbas CSV, Bellomo R, Burns KEA, Einav S, et al. Personalized mechanical ventilation in acute respiratory distress syndrome. Crit Care Lond Engl. 2021;25:250.
5. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA. 2016;315:788–800.
6. Mead J, Gaensler EA. Esophageal and pleural pressures in man, upright and supine. J Appl Physiol. 1959;14:81–3.
7. Hedenstierna G. Esophageal pressure: benefit and limitations. Minerva Anestesiol. 2012;78:959–66.
8. Pelosi P, Goldner M, McKibben A, Adams A, Eccher G, Caironi P, et al. Recruitment and derecruitment during acute respiratory failure: an experimental study. Am J Respir Crit Care Med. 2001;164:122–30.
9. Yoshida T, Amato MBP, Grieco DL, Chen L, Lima CAS, Roldan R, et al. Esophageal manometry and regional transpulmonary pressure in lung injury. Am J Respir Crit Care Med. 2018;197:1018–26.
10. Washko GR, O'Donnell CR, Loring SH. Volume-related and volume-independent effects of posture on esophageal and transpulmonary pressures in healthy subjects. J Appl Physiol. 2006;2006(100):753–8.
11. Niknam J, Chandra A, Adams AB, Nahum A, Ravenscraft SA, Marini JJ. Effect of a nasogastric tube on esophageal pressure measurement in normal adults. Chest. 1994;106:137–41.
12. Chiumello D, Gallazzi E, Marino A, Berto V, Mietto C, Cesana B, et al. A validation study of a new nasogastric polyfunctional catheter. Intensive Care Med. 2011;37:791–5.
13. Persson P, Ahlstrand R, Gudmundsson M, de Leon A, Lundin S. Detailed measurements of oesophageal pressure during mechanical ventilation with an advanced high-resolution manometry catheter. Crit Care Lond Engl. 2019;23:217.
14. Chiumello D, Consonni D, Coppola S, Froio S, Crimella F, Colombo A. The occlusion tests and end-expiratory esophageal pressure: measurements and comparison in controlled and assisted ventilation. Ann Intensive Care. 2016;6:13.
15. Mojoli F, Iotti GA, Torriglia F, Pozzi M, Volta CA, Bianzina S, et al. In vivo calibration of esophageal pressure in the mechanically ventilated patient makes measurements reliable. Crit Care Lond Engl. 2016;20:98.
16. Mojoli F, Chiumello D, Pozzi M, Algieri I, Bianzina S, Luoni S, et al. Esophageal pressure measurements under different conditions of intrathoracic pressure. An in vitro study of second generation balloon catheters. Minerva Anestesiol. 2015;81:855–64.
17. Mojoli F, Torriglia F, Orlando A, Bianchi I, Arisi E, Pozzi M. Technical aspects of bedside respiratory monitoring of transpulmonary pressure. Ann Transl Med. 2018;6:377.
18. Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J. A simple method for assessing the validity of the esophageal balloon technique. Am Rev Respir Dis. 1982;126:788–91.
19. Beda A, Güldner A, Carvalho AR, Zin WA, Carvalho NC, Huhle R, et al. Liquid- and air-filled catheters without balloon as an alternative to the air-filled balloon catheter for measurement of esophageal pressure. PLoS ONE. 2014;9:e103057.
20. Coppola S, Pozzi T, Gurgitano M, Liguori A, Duka E, Bichi F, et al. Radiological pattern in ARDS patients: partitioned respiratory mechanics, gas exchange and lung recruitability. Ann Intensive Care. 2021;11:78.
21. Pelosi P, Croci M, Ravagnan I, Vicardi P, Gattinoni L. Total respiratory system, lung, and chest wall mechanics in sedated-paralyzed postoperative morbidly obese patients. Chest. 1996;109:144–51.
22. Regli A, Pelosi P, Malbrain MLNG. Ventilation in patients with intra-abdominal hypertension: what every critical care physician needs to know. Ann Intensive Care. 2019;9:52.
23. Gattinoni L, Chiumello D, Carlesso E, Valenza F. Bench-to-bedside review: chest wall elastance in acute lung injury/acute respiratory distress syndrome patients. Crit Care. 2004;8:350.
24. Gattinoni L, Marini JJ, Collino F, Maiolo G, Rapetti F, Tonetti T, et al. The future of mechanical ventilation: lessons from the present and the past. Crit Care. 2017;21:183.
25. Gulati G, Novero A, Loring SH, Talmor D. Pleural pressure and optimal positive end-expiratory pressure based on esophageal pressure versus chest wall elastance: incompatible results*. Crit Care Med. 2013;41:1951–7.
26. Mietto C, Malbrain MLNG, Chiumello D. Transpulmonary pressure monitoring during mechanical ventilation: a bench-to-bedside review. Anaesthesiol Intensive Ther. 2015;47(Spec No):s27-37.
27. Stenqvist O, Lundin S. Lung elastance and transpulmonary pressure may be determined without using esophageal pressure measurements. Am J Respir Crit Care Med. 2014;190:120–120.
28. Persson P, Lundin S, Stenqvist O. Transpulmonary and pleural pressure in a respiratory system model with an elastic recoiling lung and an expanding chest wall. Intensive Care Med Exp. 2016;4:26.
29. Chiumello D, Cressoni M, Colombo A, Babini G, Brioni M, Crimella F, et al. The assessment of transpulmonary pressure in mechanically ventilated ARDS patients. Intensive Care Med. 2014;40:1670–8.

30. Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med. 2008;359:2095–104.
31. Pelosi P, D'Andrea L, Vitale G, Pesenti A, Gattinoni L. Vertical gradient of regional lung inflation in adult respiratory distress syndrome. Am J Respir Crit Care Med. 1994;149:8–13.
32. Cressoni M, Chiumello D, Carlesso E, Chiurazzi C, Amini M, Brioni M, et al. Compressive forces and computed tomography-derived positive end-expiratory pressure in acute respiratory distress syndrome. Anesthesiology. 2014;121:572–81.
33. Cressoni M, Gallazzi E, Chiurazzi C, Marino A, Brioni M, Menga F, et al. Limits of normality of quantitative thoracic CT analysis. Crit Care Lond Engl. 2013;17:R93.
34. Talmor D, Sarge T, O'Donnell CR, Ritz R, Malhotra A, Lisbon A, et al. Esophageal and transpulmonary pressures in acute respiratory failure. Crit Care Med. 2006;34:1389–94.
35. Boesing C, Graf PT, Schmitt F, Thiel M, Pelosi P, Rocco PRM, et al. Effects of different positive end-expiratory pressure titration strategies during prone positioning in patients with acute respiratory distress syndrome: a prospective interventional study. Crit Care Lond Engl. 2022;26:82.
36. Bikker IG, Blankman P, Specht P, Bakker J, Gommers D. Global and regional parameters to visualize the "best" PEEP during a PEEP trial in a porcine model with and without acute lung injury. Minerva Anestesiol. 2013;79:983–92.
37. Beitler JR, Sarge T, Banner-Goodspeed VM, Gong MN, Cook D, Novack V, et al. 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. JAMA. 2019;321:846–57.
38. Sarge T, Baedorf-Kassis E, Banner-Goodspeed V, Novack V, Loring SH, Gong MN, et al. 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. Am J Respir Crit Care Med. 2021;204:1153–63.
39. Silva PL, Ball L, Rocco PRM, Pelosi P. Physiological and pathophysiological consequences of mechanical ventilation. Semin Respir Crit Care Med. 2022;43:321–34.
40. Battaglini D, Robba C, Ball L, Silva PL, Cruz FF, Pelosi P, et al. Noninvasive respiratory support and patient self-inflicted lung injury in COVID-19: a narrative review. Br J Anaesth. 2021;127:353–64.
41. Carteaux G, Mancebo J, Mercat A, Dellamonica J, Richard J-CM, Aguirre-Bermeo H, et al. Bedside adjustment of proportional assist ventilation to target a predefined range of respiratory effort. Crit Care Med. 2013;41:2125–32.
42. Field S, Sanci S, Grassino A. Respiratory muscle oxygen consumption estimated by the diaphragm pressure-time index. J Appl Physiol. 1984;57:44–51.
43. Cereda M. How does one evaluate and monitor respiratory function in the intensive care unit? Evid-Based Pract Crit Care. Elsevier; 2010 [cited 2022 Nov 27]. p. 3–10. https://linkinghub.elsevier.com/retrieve/pii/B9781416054764000018
44. Beloncle F, Piquilloud L, Olivier P-Y, Vuillermoz A, Yvin E, Mercat A, et al. Accuracy of P0.1 measurements performed by ICU ventilators: a bench study. Ann Intensive Care. 2019;9:104.
45. Foti G, Cereda M, Banfi G, Pelosi P, Fumagalli R, Pesenti A. End-inspiratory airway occlusion: a method to assess the pressure developed by inspiratory muscles in patients with acute lung injury undergoing pressure support. Am J Respir Crit Care Med. 1997;156:1210–6.
46. Bertoni M, Telias I, Urner M, Long M, Del Sorbo L, Fan E, et al. A novel non-invasive method to detect excessively high respiratory effort and dynamic transpulmonary driving pressure during mechanical ventilation. Crit Care Lond Engl. 2019;23:346.
47. Bellani G, Grasselli G, Teggia-Droghi M, Mauri T, Coppadoro A, Brochard L, et al. Do spontaneous and mechanical breathing have similar effects on average transpulmonary and alveolar pressure? A clinical crossover study. Crit Care Lond Engl. 2016;20:142.
48. Blanch L, Villagra A, Sales B, Montanya J, Lucangelo U, Luján M, et al. Asynchronies during mechanical ventilation are associated with mortality. Intensive Care Med. 2015;41:633–41.
49. Garofalo E, Bruni A, Pelaia C, Liparota L, Lombardo N, Longhini F, et al. Recognizing, quantifying and managing patient-ventilator asynchrony in invasive and noninvasive ventilation. Expert Rev Respir Med. 2018;12:557–67.
50. Tonelli R, Fantini R, Tabbì L, Castaniere I, Pisani L, Pellegrino MR, et al. Early inspiratory effort assessment by esophageal manometry predicts noninvasive ventilation outcome in de novo respiratory failure. A pilot study. Am J Respir Crit Care Med. 2020;202:558–67.
51. Ball L, Robba C, Herrmann J, Gerard SE, Xin Y, Pigati M, et al. Early versus late intubation in COVID-19 patients failing helmet CPAP: a quantitative computed tomography study. Respir Physiol Neurobiol. 2022;301:103889.
52. Pelosi P, Tonelli R, Torregiani C, Baratella E, Confalonieri M, Battaglini D, et al. Different methods to improve the monitoring of noninvasive respiratory support of patients with severe pneumonia/ARDS due to COVID-19: an update. J Clin Med. 2022;11:1704.
53. Tonelli R, Cortegiani A, Marchioni A, Fantini R, Tabbì L, Castaniere I, et al. Nasal pressure swings as the measure of inspiratory effort in spontaneously breathing patients with de novo acute respiratory failure. Crit Care Lond Engl. 2022;26:70.
54. Grieco DL, Maggiore SM, Roca O, Spinelli E, Patel BK, Thille AW, et al. Non-invasive ventilatory support and high-flow nasal oxygen as first-line treatment of acute hypoxemic respiratory failure and ARDS. Intensive Care Med. 2021;47:851–66.
55. Tobin MJ, Jubran A, Laghi F. P-SILI as justification for intubation in COVID-19: readers as arbiters. Ann Intensive Care. 2020;10:156.

Publisher's Note