The oesophageal balloon for respiratory monitoring in ventilated patients: updated clinical review and practical aspects

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Measuring partitioned respiratory mechanics and quantifying lung stress and breathing effort using oesophageal manometry improves our understanding of the patient's unique respiratory physiology and allows personalisation of mechanical ventilation. https://bit.ly/41meCxw

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Abstract

There is a well-recognised importance for personalising mechanical ventilation settings to protect the lungs and the diaphragm for each individual patient. Measurement of oesophageal pressure (P_{oes}) as an estimate of pleural pressure allows assessment of partitioned respiratory mechanics and quantification of lung stress, which helps our understanding of the patient's respiratory physiology and could guide individualisation of ventilator settings. Oesophageal manometry also allows breathing effort quantification, which could contribute to improving settings during assisted ventilation and mechanical ventilation weaning. In parallel with technological improvements, P_{oes} monitoring is now available for daily clinical practice. This review provides a fundamental understanding of the relevant physiological concepts that can be assessed using P_{oes} measurements, both during spontaneous breathing and mechanical ventilation. We also present a practical approach for implementing oesophageal manometry at the bedside. While more clinical data are awaited to confirm the benefits of P_{oes}-guided mechanical ventilation and to determine optimal targets under different conditions, we discuss potential practical approaches, including positive end-expiratory pressure setting in controlled ventilation and assessment of inspiratory effort during assisted modes.

Introduction

Lung-protective ventilation is associated with better outcome in patients with acute respiratory distress syndrome (ARDS) [1, 2] and the recognised standard of care [3–5]. Plateau pressure (P_{plat}), driving pressure (ΔP) and respiratory system compliance are commonly measured bedside but do not take into account the respective contributions of the lungs and chest wall mechanics nor guarantee delivering optimal lung- and diaphragm-protective ventilation to every individual patient [6]. This is particularly relevant with significant lung inhomogeneity, when chest wall compliance is altered [7], when switching from controlled to assisted ventilation [8–11] or during difficult weaning. More advanced monitoring facilitates delivery of personalised mechanical ventilation. Pleural pressure (P_{pl}) estimated by oesophageal manometry enables measuring lung and chest wall distending pressures. This allows assessing the lungs

and chest wall mechanics independently [12, 13], limiting the stress applied to the lung parenchyma and quantifying the patient's inspiratory effort [14]. Extensive reviews exist describing the technique and applications of oesophageal pressure (P_{oes}) monitoring in critically ill patients [12, 13, 15–17]. However, new physiological and clinical insights are available and the technique has entered into clinical practice more regularly. An updated review is thus of interest. We provide a physiological and practical approach for state-of-the-art oesophageal manometry, including current evidence and considerations for guiding ventilator settings based on P_{oes}. We also discuss the position of P_{oes} monitoring in the context of other breathing effort monitoring methods and novel (future) developments.

What are the key (patho-)physiological concepts to understand when implementing oesophageal manometry?

The respiratory system consists of different structures and compartments: the airways, lung parenchyma with alveoli, pleural space, chest wall and respiratory muscles. Understanding their interaction is key to discern what drives movement of air into and outside the lungs and to understand the pressures that may aggravate lung injury. The force driving air into the alveoli must overcome opposing forces: 1) resistive pressure (P_{res}=flow×resistance) due to airway resistance to airflow and 2) elastic pressure (P_{el}=volume×elastance) due to the intrinsic elastic properties of the lungs and chest wall (figure 1). Elastic recoil describes the natural trend of the respiratory system to come back to its state of equilibrium, which is at end-expiration.

The equation of motion describes at any time the relationship between total respiratory system pressure (P_{tot}) and the elastic and resistive pressures: $P_{tot}=P_{res}+P_{el}$+initial pressure at end-expiration (P_0) or P_{tot}=(flow×resistance)+(volume×elastance)+P_0. The exact equation also contains a pressure to overcome tissue and gas inertia, which is negligible. Using oesophageal manometry, P_{el} can be partitioned into the transmural pressure of the lungs (transpulmonary pressure (P_L)) and that of the chest wall (pressure across the chest wall (P_{cw})) that are acting in series: $P_{el}=P_L+P_{cw}$. Thus, the equation of motion can be written as P_{tot}=(flow×resistance)+((volume×lung elastance)+(volume×chest wall elastance))+P_0 (figure 1). P_0 is omitted in non-ventilated subjects, since all pressures are measured relative to atmospheric pressure, or is equal to the total positive end-expiratory pressure ($PEEP_{tot}$) during mechanical ventilation. For more precise definitions, see LORING *et al.* [18].

Spontaneous breathing physiology in healthy conditions

At functional residual capacity (end-expiration), with the respiratory muscles relaxed and the mouth open, the respiratory system is at equilibrium. The lung and chest wall individual resting positions are different: lung elastic recoil pushes inwards, while chest wall elastic recoil pulls outwards. This results in a slightly negative end-expiratory P_{pl} in healthy subjects (figure 2a) [19].

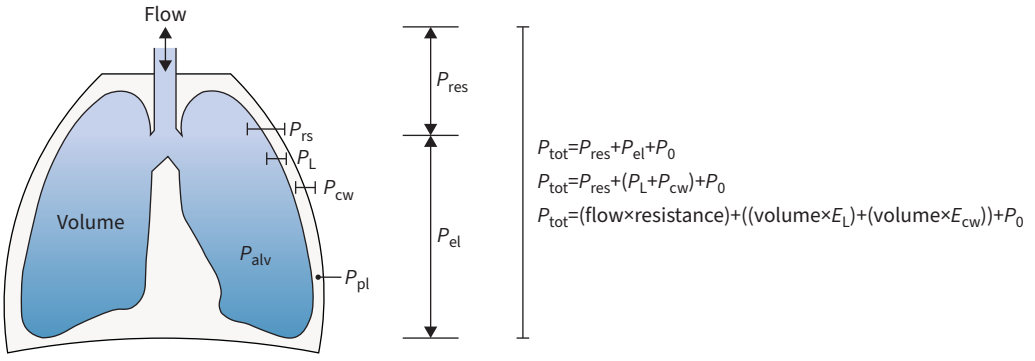


FIGURE 1 Equation of motion of the respiratory system, including the components of the lung and chest wall transmural pressures. Resistive pressure (P_{res}) is the pressure needed to overcome airway resistance. Elastic pressure (P_{el}) is the pressure needed to expand the lungs and the chest wall. P_0 is the pressure inside the respiratory system at the end of expiration, which is zero in non-ventilated patients, since all pressures are measured relative to atmospheric pressure, or is referred to as total positive end-expiratory pressure in ventilated patients. P_{alv}: alveolar pressure; P_{rs}: transmural pressure of the respiratory system (transrespiratory system pressure); P_L: transmural pressure of the lungs (transpulmonary pressure); P_{cw}: transmural pressure of the chest wall (pressure across the chest wall); P_{pl}: pleural pressure; E_L: lung elastance; E_{cw}: chest wall elastance.

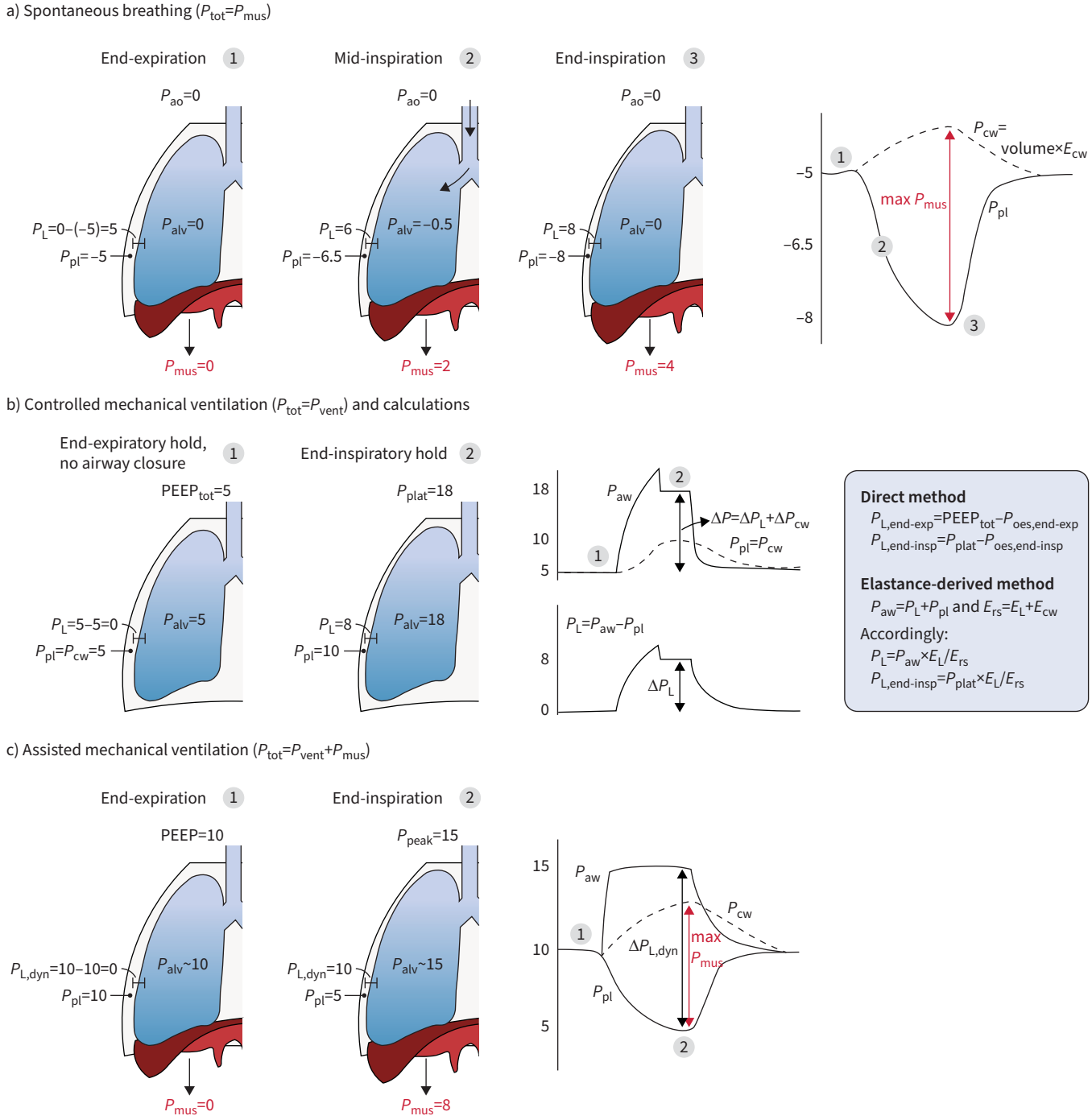


FIGURE 2 Conceptual illustrations of key respiratory physiology during a) spontaneous breathing in a non-ventilated subject, b) fully controlled mechanical ventilation with a passive patient and c) assisted mechanical ventilation. For full description, see main text. All pressures are described in cmH_2O. a) During spontaneous breathing in healthy conditions, pleural pressure (P_{pl}) is slightly negative at the end of expiration (situation 2). The pressure generated by the respiratory muscle pump (P_{mus}) creates a further drop in P_{pl}. P_{pl} is transmitted to the alveoli resulting in a negative alveolar pressure (P_{alv}) and a pressure gradient between the airway opening pressure (P_{ao}) and P_{alv} allowing tidal volume to enter (situation 2). P_{mus} is the pressure needed to generate chest wall expansion as well as a drop in P_{pl}; therefore, P_{mus} is the difference between the chest wall pressure (P_{cw}) and the P_{pl}, and maximum P_{mus} occurs at the end of inspiration (situation 3). P_{cw} is calculated by multiplying the instantaneous lung volume by the chest wall elastance (E_{cw}). E_{cw} can be obtained during passive lung inflation or calculated as 4% of predicted vital capacity [20]. b) During passive ventilator insufflation P_{pl} increases and represents the P_{cw}. Circuit occlusions are required to assess static transmural pressure of the lungs (transpulmonary pressure (P_L)). When there is no flow and with the airways fully open, P_{alv} represents the airway pressure (P_{aw}) during the occlusion: total positive end-expiratory pressure ($PEEP_{tot}$) and plateau pressure (P_{plat}) for end-expiratory and end-inspiratory occlusions, respectively. P_{plat} is thus the sum of the P_L and P_{cw} during the end-inspiratory occlusion. Likewise, the respiratory system driving

pressure (ΔP=P_{plat}−$PEEP_{tot}$) includes both the lung driving pressure (ΔP_L) and the driving pressure expanding the chest wall (ΔP_{cw}). The direct method and elastance-derived method to calculate P_L are presented. c) During assisted mechanical ventilation, both the ventilator pressure (P_{vent}) and P_{mus} contribute to lung inflation. The swing in dynamic P_L ($\Delta P_{L,dyn}$) is computed as peak P_L−end-expiratory P_L and therefore is different from the static ΔP_L (circuit occlusions), which can be difficult to obtain/read in actively breathing patients. P_{alv} is thus not necessarily equal to P_{aw} at end-expiration and end-inspiration. P_{oes}: oesophageal pressure; E_{rs}: respiratory system elastance; E_L: lung elastance.

During spontaneous breathing without ventilatory assistance, inspiratory muscle contraction generates a muscle pressure (P_{mus}) that pulls the chest wall further outwards; P_{pl} thus decreases to a more negative value. P_{pl} is transmitted to the alveoli resulting in a pressure gradient between atmospheric pressure (airway opening pressure (P_{ao})) and the alveolar pressure (P_{alv}); this drives air into the lungs, allowing tidal volume (V_T) to enter. Therefore, during spontaneous breathing the only source of pressure is P_{mus} (*i.e.* P_{tot}=P_{mus}) and inflow occurs whenever the P_{ao}–P_{alv} gradient is >0 (figure 2a).

Of note, during active inspiration, the pressure generated by the relaxed chest wall (*i.e.* P_{cw}) has to be overcome before airflow can start. P_{cw} can only be measured during completely passive lung inflation. In this situation, P_{pl} increases, representing the pressure generated by the chest wall recoil at the specific volume. P_{cw} can also be computed as the instantaneous volume divided by the theoretical chest wall compliance (estimated as 4% of predicted vital capacity [20]). P_{mus} represents the difference between P_{cw} and the change in P_{pl} throughout the breathing effort, with maximal tidal P_{mus}=(V_T×chest wall elastance)−ΔP_{pl} (figure 2a). Thus, to quantify the magnitude and timing of P_{mus}, estimation of P_{pl} *via* oesophageal manometry is required [21].

Physiology during mechanical ventilation

Controlled mechanical ventilation

In passively ventilated patients, the only pressure source is the ventilator: P_{tot}=P_{vent}. Without airway flow (no resistive pressure) as during circuit occlusions, and in the absence of airway collapse, airway pressure (P_{aw}) measured by the ventilator equals P_{alv}. Estimation of P_{pl} then allows for quantification of the static transmural pressure of the lungs (P_L=P_{aw}−P_{pl}; direct measurement technique, see later) and of the chest wall (P_{cw}=P_{pl}−P_{atm}=P_{pl}−0=P_{pl}) (figure 2b).

During a ventilator breath, P_L has temporal and spatial variations. Maximal P_L occurs at end-inspiration when total V_T has entered the lungs: P_{alv} then equals P_{plat}, measured during a short end-inspiratory occlusion. P_{plat} reflects the pressure that distends both the lungs and chest wall: P_{plat}=$P_{L,end\text{-}insp}$+$P_{cw,end\text{-}insp}$ (measured during end-inspiratory occlusion). Likewise, the respiratory system driving pressure (ΔP=P_{plat}−$PEEP_{tot}$) includes both the lung driving pressure (*i.e.* ΔP_L) and the driving pressure expanding the chest wall (ΔP_{cw}) (figure 2b). Thus, for the same P_{plat} and ΔP, end-inspiratory P_L and ΔP_L differ according to the respective lung and chest wall elastances (elastance=1/compliance) [22]: higher lung elastance ("stiff" lung) will result in higher P_L and ΔP_L, while higher chest wall elastance ("stiff" chest wall) will result in lower P_L and ΔP_L (but higher P_{cw}). Regarding the spatial variations of P_L, P_L is higher in the non-dependent lung compared with the dependent regions; this gradient is exacerbated in ARDS. In this situation, for a given "global" P_L value (estimated with P_{oes}, which does not include the spatial gradient), overdistension in the non-dependent lung units can occur concomitantly with collapse and atelectrauma in the dependent units.

In practice, two main methods exist to calculate P_L from P_{oes} (figure 2b). The so-called direct method [22, 23] computes P_L as the absolute difference between P_{alv} (that equals P_{aw} during circuit occlusions) and P_{oes}. The elastance-derived method [24, 25] uses the tidal change in P_{oes} (measured with circuit occlusions) to calculate the ratio between lung elastance (E_L) and respiratory system elastance (E_{rs}); P_L is then calculated as P_{aw}×E_L/E_{rs} (see supplementary material). This approach assumes that changes in P_{pl} and P_{oes} are similar while their absolute values may differ. Both calculation methods are based on assumptions with possible errors. Experimental work in human cadavers and a porcine model of ARDS demonstrated that absolute P_{oes} accurately reflected local P_{pl} close to the measurement site (middle third of the oesophagus), corresponding to the mid-dorsal regions of the human thorax [26]. Therefore, the direct method is deemed useful to estimate P_L in the mid-dependent lung regions. Importantly, this remains true with asymmetrical lung injury, where P_{pl} equalises across the two lungs [27]. In contrast, P_L calculated with the elastance-derived method better reflected lung distending pressure of non-dependent regions [26]. Both methods therefore may have different clinical meanings in P_{oes}-guided mechanical ventilation (see later).

Assisted mechanical ventilation

During assisted mechanical ventilation (assist-controlled or purely assisted), the force driving lung inflation and chest wall expansion depends on the combination of the pressure provided by the ventilator and the spontaneous breathing effort: $P_{tot}=P_{vent}+P_{mus}$. Therefore, during assisted ventilation it is key to understand that the pressures displayed on the ventilator monitor only reflect part of the total pressure applied to the alveoli: P_L results from both P_{aw} and P_{mus} (figure 2c).

A brief history of oesophageal pressure monitoring

In 1949, Buytendijk [28] introduced the latex air-filled oesophageal balloon to study the dynamic lung elasticity in various pulmonary diseases and healthy lungs in 150 subjects. Long before that, in 1878–1880, Luciani and Rosenthal described a minimally invasive extrapleural assessment of pleural pressure by placing an open cannula in the oesophagus (cited in [28]). However, since the holes of the catheter tip were not covered with a balloon, this cannula could clog easily and the air-filled latex balloon was introduced by Buytendijk [28] as a solution to protect the catheter from oesophageal mucus while measuring pressure changes. This increased the popularity of the technique, which was further improved for assessment of both dynamic and passive respiratory mechanics in the years that followed [29–33]. With the more recent improvements of catheters, transducers and bedside monitors facilitating easy catheter insertion, use and calibration, the technique has now moved from a research tool towards a clinical modality at the bedside.

Oesophageal pressure: how do we measure it?

A practical step-by-step description of oesophageal manometry is provided in figure 3 and detailed in the following subsections.

Catheter and equipment

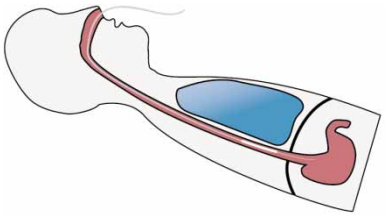
A variety of catheters equipped with oesophageal balloons are available for P_{oes} measurement (see supplementary figure S1 for the most commonly used catheters and Mojoli *et al.* [34] for all second-generation catheters). Some catheters are endowed with a gastric balloon for simultaneous measurement of gastric pressure. Prior to insertion (patient in semi-recumbent position), the balloon is checked for leaks by air inflation, deflated and connected to a three-way stopcock. Rigid tubing should be used to avoid underestimation of pressures due to signal dampening and phase lag (because of non-rigid tube compliance). This is especially important when fast pressure changes are of interest such as during spontaneous efforts. The catheter with extension tubing is then attached to a pressure transducer and connected to a bedside monitor or mechanical ventilator (for some examples, see supplementary figure S2); the pressure waveform should show zero pressure with an open system. Note that commonly used haemodynamic transducers are often calibrated for the positive pressure range (or including a small negative range); hence, they are especially valuable for measuring P_{oes} under passive conditions but may slightly underestimate effort in the presence of excessive negative pressures. A dedicated system for measuring P_{oes} or an auxiliary pressure port of a ventilator can also be used.

Inserting and filling the balloon

The catheter is gently advanced into the mid-lower third part of the oesophagus, commonly at a depth of 33–40 cm from the nostril [35]. Alternatively, it could be advanced into the stomach and then withdrawn in small steps; positive deflections in P_{oes} tracing following gentle epigastric pressure verify intragastric balloon positioning. Oesophageal placement is verified by the presence of cardiac oscillations in P_{oes} tracing [35] and by an occlusion test (see later). To perform the position check and measurements, the balloon is inflated with air. Balloon filling involves complete balloon deflation, equilibration at atmospheric pressure *via* brief disconnection, injection of maximum air volume to homogenously stretch its walls and then deflation to optimum filling volume (V_{best}). In theory, V_{best} is the minimum volume at which tidal P_{oes} swings are maximum [36], which depends on the balloon's structural properties (length, diameter and compliance), the surrounding intrathoracic pressure and body position/gravity, but also varies depending on whether the patient is on passive mechanical ventilation or spontaneously breathing. Both too low and too high filling volume dampens tidal P_{oes} swings. Furthermore, compression of the balloon with too low filling volume may result in emptying of the balloon in the catheter–tubing–transducer system and underestimates baseline P_{oes}. In contrast, too high filling volume results in an abrupt baseline increase and thus overestimation of P_{oes}: since walls of the relaxed oesophagus are normally apposed, distention by too much air produces a positive pressure [29], reflecting elastic recoil of an overfilled balloon. Long, wide balloons have a wider range of V_{best} [12, 30, 31], and thin wall balloons have higher compliance and transmit P_{oes} more precisely. In practice, we suggest using the volume proposed by the manufacturer as an initial volume and adjust accordingly, if deemed necessary depending on the occlusion test [35]. Importantly, with intrathoracic pressure increases (*e.g.* high PEEP, high ΔP in conditions of high lung

1 Prepare materials
- *Collect*: oesophageal catheter, 2–5 mL syringe, three-way stopcock, rigid extension tubing, pressure transducer and/or dedicated module
- Check for balloon leaks by air inflation and deflation

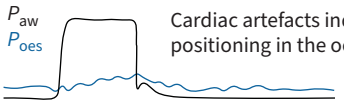
2 Insert catheter and connect to monitor
Usually 33–40 cm from the nostril to position the balloon in the mid-lower third part of the oesophagus
Alternative: advance catheter into stomach and withdraw in small steps



- Placement is easier in semi-recumbent position
- Water-soluble lubricant aids insertion
- Pay attention to coughing or air leaking around the endotracheal tube, this may suggest tracheal insertion
- Depth markings aid in positioning
- Connect the catheter with the extension tubing and three-way stopcock to the pressure port and/or dedicated monitor

3 Inflate the balloon
- Attach the syringe and pull out any air from the balloon
- Equilibrate the system to ambient pressure: P_{oes} should be zero with the three-way stopcock open to air
- Inject maximum air volume and deflate to optimum volume; start with initial volume as described by the manufacturer: Cooper: 2 mL in, 1.2 mL out; NutriVent: 4 mL in, 1.5 mL out

4 Verify cardiac oscillations in the P_{oes} tracing

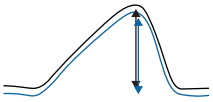


Cardiac artefacts indicate positioning in the oesophagus

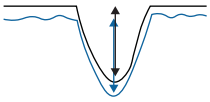
If P_{oes} and P_{aw} waveforms look similar and if P_{oes} and P_{aw} values are exactly the same during occlusions, the balloon was probably inserted into the trachea. Deflate and remove the balloon and insert again.

5 Confirm accuracy of P_{oes} monitoring with the occlusion test

Passive patient
1) Perform an end-expiratory occlusion
2) Apply a gentle bilateral thoracic compression
3) Measure the increase in P_{aw} and P_{oes}



Actively breathing patient
1) Perform an end-expiratory occlusion
2) Wait for the next occluded inspiratory effort
3) Measure the decrease in P_{aw} and P_{oes}



4) Check if $\Delta P_{aw}/\Delta P_{oes}$ ratio is within the 0.8–1.2 range
The closer the ratio is to 1, the more precise the P_{oes} measurement is
Out of range? Adjust the catheter position and/or filling volume until accuracy is confirmed

6 Check the plausibility of P_{oes} values
If baseline P_{oes} is very high, suspect balloon overinflation: deflate the balloon, reinflate and repeat the occlusion test with less air in the balloon

7 Secure the catheter and start P_{oes} measurements
Passive patient: perform end-expiratory and end-inspiratory occlusions to measure P_{oes} and P_L
Actively breathing patient: measure dynamic changes in P_{oes} and P_L

*Repeat Step **5** regularly to confirm accuracy of P_{oes} measurements, especially after changes in ventilator settings, respiratory mechanics or body position*

FIGURE 3 Oesophageal manometry: a practical step-by-step approach to oesophageal pressure (P_{oes}) measurements in clinical practice. For further clinical and scientific details, see main text. P_{aw}: airway pressure; P_L: transmural pressure of the lungs (transpulmonary pressure).

elastance and supine position), V_{best} may be higher than suggested [34, 36, 37]. It is thus important to periodically confirm the accuracy of the measurements by repeating the occlusion test, especially following significant changes in ventilator settings, respiratory mechanics or body position.

Occlusion test: confirming accuracy of measurement

Adequate balloon filling volume and position should be confirmed with an occlusion test before interpreting P_{oes} values. During a circuit occlusion and in the absence of airway closure, P_{aw}=P_{alv}. Moreover, in a closed compartment pressure changes are equally transmitted to the different anatomical components. Then, any change in P_{aw}, P_{pl} and P_{oes} should be of similar amplitude. Verification of this assumption is used to confirm the validity of P_{oes} to estimate P_{pl} and requires a different manoeuvre when the patient is spontaneously breathing compared with a passive patient. With breathing efforts, a dynamic occlusion test, *i.e.* Baydur manoeuvre, is required [13]: an end-expiratory hold is performed and the next inspiratory effort generates a decrease in P_{aw} and P_{oes} against the closed valve. It does not require the patient's collaboration but can induce some discomfort in awake patients. The ratio of the P_{aw} and P_{oes} drop ($\Delta P_{aw}/\Delta P_{oes}$) during the occluded breath must be close to unity (between 0.8 and 1.2 [13, 38], accepting a 20% error, or ideally between 0.9 and 1.1 for higher accuracy). In passive patients, an external gentle slow manual bilateral thoracic compression is performed during an end-expiratory occlusion to confirm that the $\Delta P_{aw}/\Delta P_{oes}$ ratio is within the required range. During this positive pressure occlusion test, P_{aw} and P_{oes} increase similarly if P_{oes} is reliable [39]. When the P_L tracing is displayed on the screen, a flat P_L during the occlusion test also confirms that $\Delta P_{aw}/\Delta P_{oes}$ is 1.

The occlusion test has been validated both in adults and children [38–40]. Since different factors can influence the balloon filling volume and thus $\Delta P_{aw}/\Delta P_{oes}$ ratio, it is recommended to systematically check the reliability of the P_{oes} measurement before interpreting values and reposition the balloon and/or adjust the filling volume until validity is confirmed [30, 38]. Regularly checking the $\Delta P_{aw}/\Delta P_{oes}$ ratio is also important during continuous trend monitoring of P_{oes} and/or P_L, since the balloon may empty over time.

Artefacts

Peristaltic oesophageal contractions or spasms generate slow and large amplitude increases in P_{oes} unrelated to the respiratory cycle; reading of P_{oes} values should be postponed until the signal stabilises. Cardiac contractions transmitted to the balloon can slightly distort the P_{oes} signal that nevertheless usually can still be read. Optimal removal of cardiac artefacts is a topic of research [41, 42]; practically, it is recommended to take end-inspiratory and end-expiratory P_{oes} values at the same time-point within the artefact.

How do we monitor and guide mechanical ventilation and in whom?

Applications during passive mechanical ventilation

Setting PEEP to avoid atelectrauma and lung collapse

Partial or complete lung tissue collapse is reflected by negative end-expiratory P_L. Negative P_L implies atelectasis, increased lung heterogeneity and intrapulmonary shunt, and decreased end-expiratory volumes (at which lung elastance is higher). Increasing PEEP to obtain slightly positive end-expiratory P_L (calculated with the direct method as $PEEP_{tot}$−end-expiratory P_{oes}, measured with occlusions) allows keeping the alveoli open at end-expiration. This approach could be of interest in ARDS or in patients with elevated P_{pl} from other causes (*e.g.* abdominal hypertension, ascites, pleural fluids, thoracic wall abnormalities and sometimes obesity). Since the absolute P_{oes} value approximates the actual P_{pl} particularly well in the dependent lung regions at highest risk of collapse, P_{oes}-guided PEEP setting should optimise recruitment and decrease atelectrauma in these regions. Importantly, given the spatial differences in P_{pl}, clinicians must consider the possibility of overdistension in the non-dependent lung regions at the selected PEEP value.

Two randomised controlled trials in ARDS compared P_{oes}-guided PEEP setting and PEEP–inspiratory oxygen fraction (F_{IO_2}) tables. In the small single-centre EPVent-1 trial, P_{oes}-guided PEEP setting titrated to positive end-expiratory P_L resulted in higher PEEP at 72 h (mean 17 *versus* 10 cmH_2O for P_{oes}-guided *versus* low PEEP–F_{IO_2} table strategy) and improved oxygenation and compliance [23]. A trend towards better clinical outcome was also reported (but underpowered for mortality). The study was terminated early (n=61) because of improved oxygenation on interim analysis. The larger multicentre EPVent-2 trial (n=200, composite primary end-point incorporating mortality and ventilator-free days at day 28) did not find clinical benefits of targeting positive end-expiratory P_L of 0–6 cmH_2O compared with empirical high PEEP (high PEEP–F_{IO_2} table) [43]. The fact that PEEP and P_{plat} between groups were similar during the first week and higher compared with other ARDS trials [44], and that P_{oes}-guided PEEP setting resulted in rather high end-expiratory P_L, could have contributed to the discrepancy with EPVent-1 results. Recent post-hoc reanalysis of EPVent-2 suggested better survival with P_{oes}-guided PEEP in patients having lower Acute Physiology and Chronic Health Evaluation (APACHE) II score (less severe multiple organ failure) and that benefits could be maximised by targeting end-expiratory P_L tightly within 0±2 cmH_2O compared

with higher or more negative values [45]. Experimental work suggests that this strategy optimises the trade-off between lung collapse and overdistension also in unilateral lung injury [27].

Limiting stress applied to the lung

During tidal inflation the stress applied to the lung parenchyma must be as low as possible to avoid ventilator-induced lung injury (VILI) [4, 46]. Although P_{plat} and ΔP limitations are cornerstones of lung-protective ventilation, these parameters do not reflect lung stress due to interpatient variability in the E_L/E_{rs} ratio [47]. Titration of end-inspiratory P_L and ΔP_L could allow delivering optimised lung-protective ventilation [7, 48], and is of particular interest in patients with elevated P_{pl} due to impaired chest wall mechanics [35, 43] and in severe ARDS with high lung elastance (small baby lung).

As previously mentioned, experimental work suggests that maximal P_L of non-dependent regions is best reflected by end-inspiratory P_L calculated with the elastance-derived method [26]. Targeting elastance-derived end-inspiratory P_L <25 cmH_2O to guide safe PEEP increases while preventing injurious lung stress was tested in 14 patients with ARDS due to influenza H1N1 infection referred for extracorporeal membrane oxygenation (ECMO) [7]. Seven patients (50%) showed increased chest wall elastance resulting in a wide gap between P_{plat} and end-inspiratory P_L; in this subgroup, increasing PEEP using a P_{oes}-guided strategy up to the target P_L improved oxygenation and prevented the use of ECMO without increasing mortality [7].

End-inspiratory P_L <25 cmH_2O measured with the direct method closely reflects P_L at total lung capacity in healthy volunteers, suggesting that this threshold could be too high to prevent VILI in non-dependent regions in inhomogeneous lungs [49]. In the EPVent-2 study, end-inspiratory P_L <20 cmH_2O (direct method) was targeted but no effect on outcome compared with the control group was demonstrated [43]. Considering normal values at different lung volumes in healthy volunteers [49] and the risk of increased local stress in heterogeneous lungs, the end-inspiratory P_L threshold calculated with the direct method should probably be <20 cmH_2O, at least in patients with inhomogeneous lungs. This, however, requires new clinical studies. Additionally, given that limiting ventilation to a target end-inspiratory P_L aims at reducing overdistension in the non-dependent (aerated baby) lung, it is physiologically sound to use the elastance-derived method to calculate this parameter. As an alternative to using end-inspiratory P_L and based on physiological reasoning, conservative targets for ΔP_L have been proposed as <15–20 cmH_2O in healthy lungs and <10–12 cmH_2O for ARDS [13, 35]. Complementary reanalysis of EPVent-1 data (n=56) reported lower ΔP_L in the intervention group at 24 h after enrolment, associated with improved 28-day mortality [48].

A summary of P_{oes}-guided ventilation targets for ARDS and their level of evidence is provided in figure 4.

Specific population: obesity

Morbid obesity can be associated with elevated P_{pl} due to excess load imposed by the weight of the chest wall. This is frequently associated with preserved chest wall compliance [50–52] but smaller lung volumes [53]. In the situation of obesity, airway pressures can sometimes be high and P_{plat} values traditionally considered unsafe in ARDS may be associated with safe P_L. End-inspiratory P_L more accurately reflects the risk of lung stress in obesity [54]. Compared with a conventional approach, P_L-guided lung-protective ventilation in obese patients aiming for positive end-expiratory P_L overall led to higher PEEP and restored end-expiratory volumes, improved lung elastance and oxygenation, prevented lung overdistention, and was haemodynamically tolerated [55–59]. It also decreased ARDS mortality in patients with body mass index (BMI) >40 $kg \cdot m^{-2}$ [60]. It is important to underline that, despite significant correlations between BMI and absolute P_{oes} values, there is no validated tool to estimate interindividual variability in P_L or chest wall compliance without measuring P_{oes} in obese patients [50]. Hence, an oesophageal balloon is needed to demonstrate whether high P_{plat} values are safe in obesity.

Determination of lung and chest wall elastance and compliance

Besides titrating ventilator pressures, oesophageal manometry allows measuring and monitoring of static lung and chest wall compliance. The formulas are given in the supplementary material.

Applications for the active patient

Breathing effort monitoring

Monitoring dynamic change in P_{oes} (ΔP_{oes} or P_{oes} swing) is the most commonly used and readily available parameter for breathing effort estimation. However, ΔP_{oes} underestimates P_{mus} (see earlier for calculation) that includes the effort needed to move both the chest wall and the lungs (figure 2a). Whereas P_{mus} represents the pressure generated by all inspiratory muscles, the transdiaphragmatic pressure (P_{di}) is specific

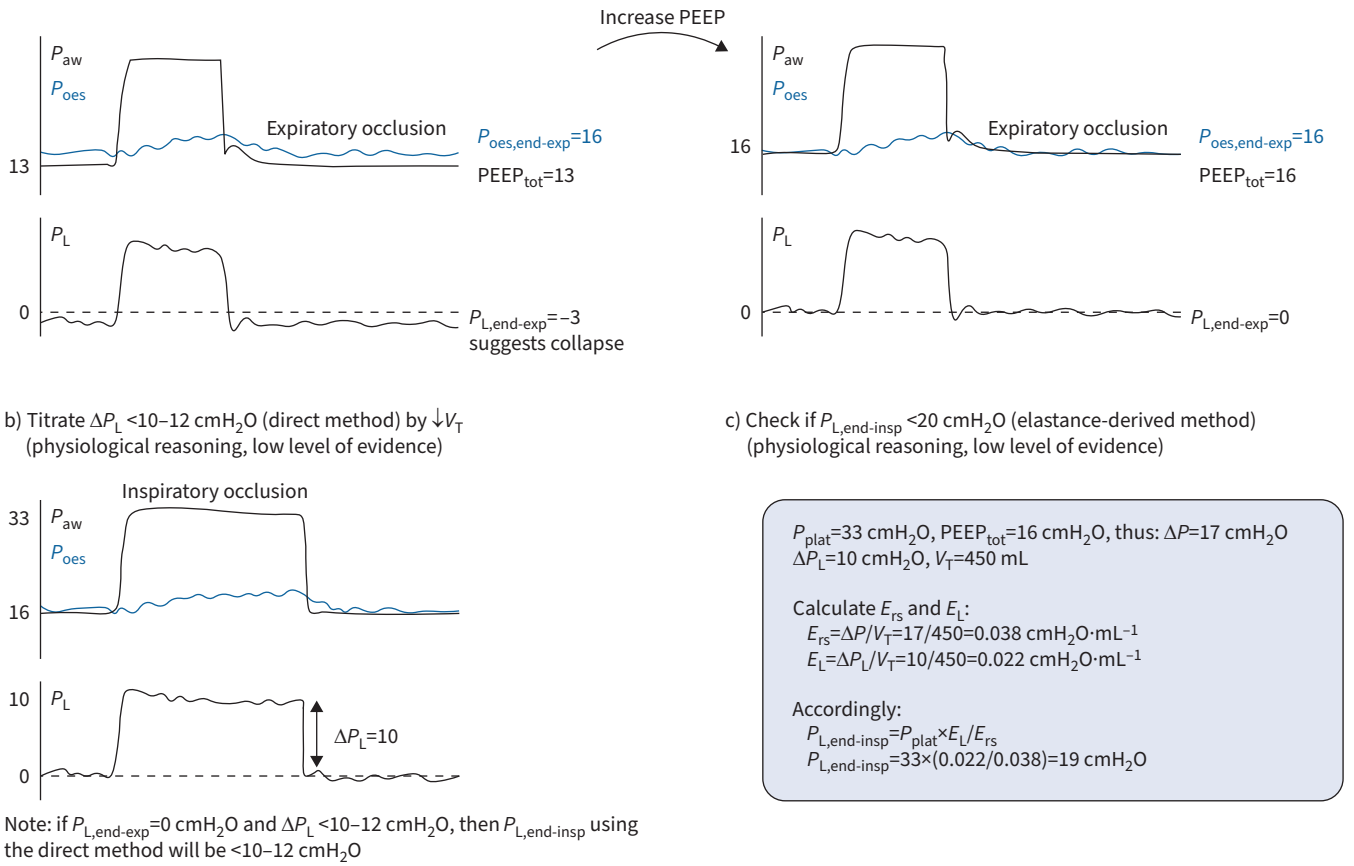


FIGURE 4 Summary of suggested steps for oesophageal pressure (P_{oes})-guided titration of mechanical ventilation in acute respiratory distress syndrome during controlled mechanical ventilation. The procedure should be performed sequentially with step a), then step b) and finally step c). The level of evidence is mentioned. All pressures are described in cmH_2O. P_L: transmural pressure of the lungs (transpulmonary pressure); PEEP: positive end-expiratory pressure; P_{aw}: airway pressure; $P_{oes,end-exp}$: end-expiratory P_{oes}; $PEEP_{tot}$: total PEEP; V_T: tidal volume; $P_{L,end-exp}$: end-expiratory P_L; $P_{L,end-insp}$: end-inspiratory P_L; P_{plat}: plateau pressure; E_{rs}: respiratory system elastance; E_L: lung elastance.

to the diaphragm and requires a double-balloon catheter to measure gastric pressure (P_{ga}) and P_{oes} simultaneously: $P_{di}=P_{ga}-P_{oes}$ (figure 5); P_{di} swing is a good estimation of effort provided that there is no significant accessory inspiratory muscle recruitment. ΔP_{oes} 3–12 cmH_2O, ΔP_{mus} 3–15 cmH_2O and ΔP_{di} 5–15 cmH_2O are considered physiological ranges of effort during assisted ventilation [6, 61], but defining a "safe" range, especially upper limits, requires further study. Nevertheless, too low values may suggest ventilator over-assist and risk of diaphragmatic atrophy (strong clinical evidence [62–65]), whereas high values may cause "overuse" diaphragmatic injury (limited evidence, mostly experimental [66–69]). Recent physiological trials demonstrated the feasibility of titrating ventilator support and/or sedation to achieve lung- and respiratory muscle-protective targets [11, 70]; larger studies should evaluate effects on clinical outcomes.

Estimation of inspiratory effort with P_{oes} and/or P_{mus} may be challenging in the presence of expiratory muscle activity. Significant expiratory muscle activity during expiration increases intra-abdominal and intrathoracic pressure (and thus P_{pl}), and subsequent expiratory muscle relaxation at the end of expiration results in a decrease in P_{pl}; this pressure drop should be corrected for when calculating inspiratory muscle effort of the next inspiration [71, 72]. Practically, recording the increase in P_{ga} during expiration is required to quantify expiratory muscle effort, if present [73, 74], and must be subtracted from ΔP_{oes} of the next inspiration.

The amplitude of P_{oes} swings neglects the time component of muscle contraction and does not account for intrinsic PEEP ($PEEP_i$) if present (see later). Work of breathing (WOB) and the oesophageal pressure–time product (PTP_{oes}) integrate these aspects [14], but are seldom used clinically due to their complexity. WOB is obtained by calculating the area of the volume–pressure (P_{oes} or P_{di}) curve, also known as the Campbell

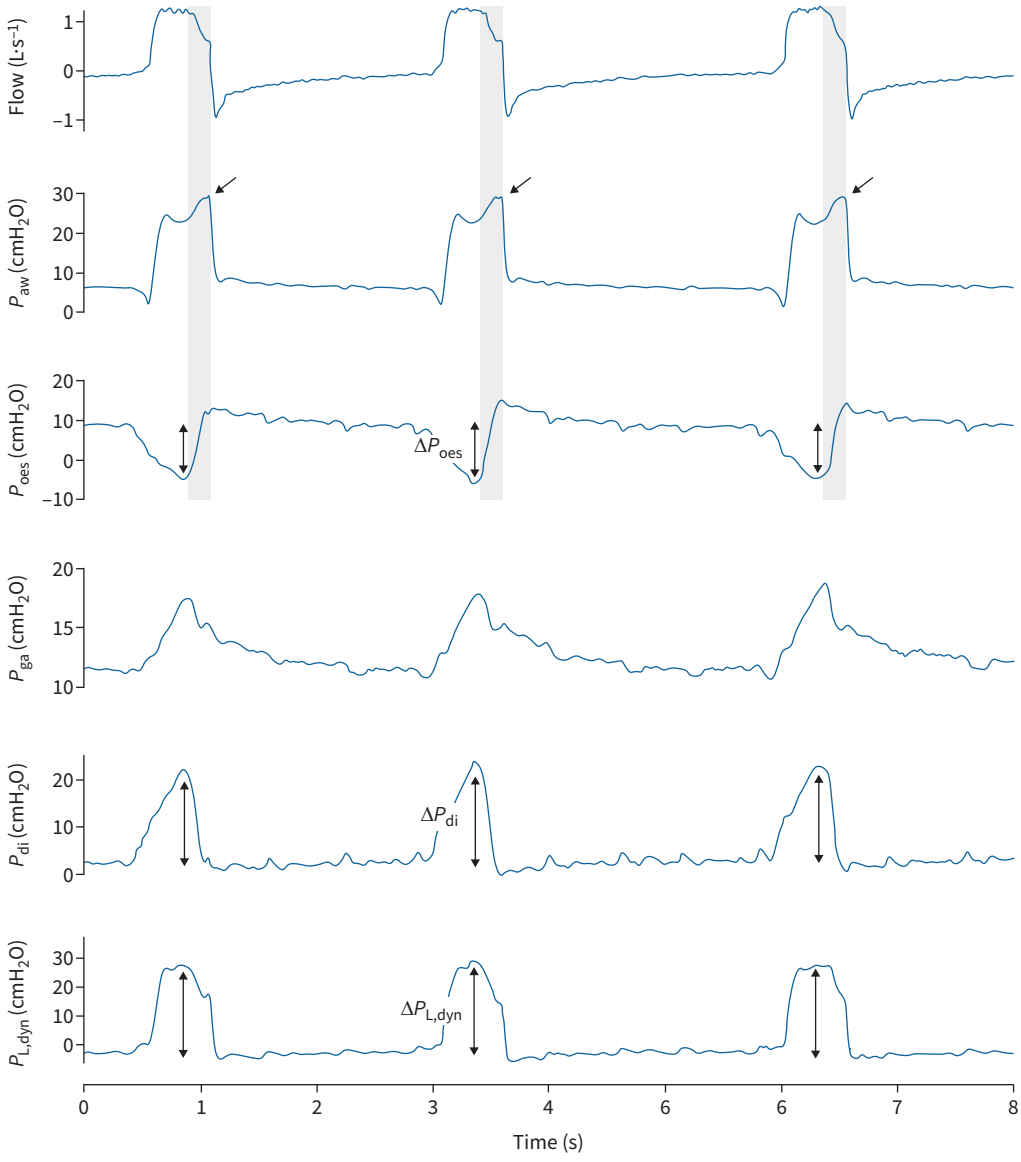


FIGURE 5 Example of oesophageal manometry during assisted mechanical ventilation. A double-balloon naso-gastric catheter was inserted for simultaneous measurement of oesophageal pressure (P_{oes}) and gastric pressure (P_{ga}) and the resulting transdiaphragmatic pressure (P_{di}). Dynamic transpulmonary pressure ($P_{L,dyn}$) was obtained in real-time as airway pressure (P_{aw})–P_{oes}. P_{oes} measurements revealed patient–ventilator asynchrony delayed cycling-off (grey area and arrows in P_{aw} signal): at the time of ventilator cycling-off, P_{oes} and P_{di} were already back to their baseline value, indicating that the patient's neural inspiratory time was shorter than the ventilator inspiratory time. In addition, the patient demonstrated high breathing effort with P_{oes} swings of 15 cmH$_2$O and P_{di} swings of 20 cmH$_2$O, resulting in $\Delta P_{L,dyn}$ >25 cmH$_2$O. Note that the end of neural inspiratory time (start of grey area) is presented just after the nadir in P_{oes}, but the exact timing is debatable.

diagram [14, 75], and only includes effort resulting in volume displacement. PTP_{oes} refers to the time integral of P_{oes}, taking into account P_{cw}, and thus incorporates isometric and miometric effort [76]. PTP_{oes} correlated to oxygen consumption of the respiratory muscles [77]. For more details, see supplementary figure S3 and an extensive review by DE VRIES *et al.* [78].

Estimation of lung stress

Inhomogeneous distribution of lung stress during spontaneous breathing may play an important role in the development or worsening of lung injury, especially with severe "solid-like" injury [79–81]. Through the

pendelluft phenomenon in inhomogeneous lungs (*i.e.* gas distributed between different lung regions without change in V_T), strong inspiratory efforts can augment regional lung stress and strain while P_{aw} and V_T remain the same [82]. In contrast, in mild lung injury spontaneous breathing was found beneficial for lung recruitment [83, 84].

Inspiratory changes in dynamic P_L ($\Delta P_{L,dyn}$) could estimate dynamic lung stress (figure 5). Measurement requires the P_L waveform displayed in real-time. $\Delta P_{L,dyn}$ is generally computed as peak P_L−end-expiratory P_L and therefore is different from the static ΔP_L (circuit occlusions), which can be difficult to obtain/read in actively breathing patients [85]. If inspiratory occlusions can be reliably obtained, the plateau phase of $P_{L,dyn}$ is thought to best represent stress on the non-dependent lung, whereas $\Delta P_{L,dyn}$ likely reflects approximately the maximum dependent lung stretch [86]. $\Delta P_{L,dyn}$ upper safe limits are uncertain, but values <15–20 cmH_2O were proposed [61]; however, they probably depend on lung injury severity and systemic inflammation.

Quantification of dynamic hyperinflation and PEEP$_i$

With dynamic hyperinflation, inspiratory effort is required to overcome $PEEP_i$ before volume displacement. Quantification of $PEEP_i$ requires measuring the P_{oes} drop before inspiratory flow starts (supplementary figure S3). With co-occurrence of expiratory muscle activity and $PEEP_i$, which may be common in patients with COPD [72], additional P_{ga} monitoring is recommended; P_{ga} drop owing to expiratory muscle relaxation at the next inspiration should be subtracted from ΔP_{oes} to avoid $PEEP_i$ overestimation [72].

Assessment of patient–ventilator interaction

Patient–ventilator asynchronies arising from temporal or quantitative dissociation between the neural breath and ventilator-delivered pressurisation could potentially be harmful [87–89]. Careful inspection of P_{aw}–time and flow–time waveforms is encouraged to identify their presence to optimise ventilator settings accordingly [90]. This requires expertise and can be challenging or sometimes impossible [91]. Auto-triggered breaths, triggering delay, ineffective efforts around the cycling-off, reverse triggering and early or delayed cycling-off are very difficult to detect without monitoring patient effort, as well as triggering resulting from expiratory muscle relaxation [92]. Automated machine algorithms may increase the accuracy of waveform inspection [93–97], but continuous P_{oes} monitoring remains the most precise method for identifying dyssynchrony (figure 5) and quantifying the magnitude and timing of dyssynchronous efforts and their impact on lung stress. It also enables direct assessment of adjustments in ventilator settings on patient–ventilator interaction.

Weaning

Both predicting weaning failure [98, 99] and enhancing mechanical ventilation weaning [100] remain important challenges to improve outcomes. Measurements of P_{mus}, PTP_{oes} and WOB are of interest as respiratory effort has been shown to increase markedly during a failed weaning trial [101, 102]. In addition, expiratory muscle activation may contribute to respiratory muscle effort in weaning failure and could be recognised with P_{oes} and P_{ga} monitoring [73]. P_{oes} trend monitoring during weaning trials performed better than the rapid shallow breathing index to predict weaning failure [103]. P_{oes} monitoring can thus be used to detect weaning failure early during the weaning trial. This could help treating potential reversible factors such as lung oedema, pain or anxiety, allows stopping earlier a spontaneous breathing trial that is going to fail and thus may potentially contribute to avoiding diaphragm injury due to diaphragm overuse. Conceptually, P_{oes} monitoring during weaning seems of interest but additional studies are needed before recommending it as standard of care. P_{mus}, PTP_{oes} and WOB values associated with weaning failure also have to be determined.

Is the oesophageal balloon gold standard?

Despite its introduction a few decades ago and its potential interest as outlined in this review, the oesophageal balloon is only starting to be used regularly in clinical practice, in parallel with technical improvements including the recording systems. Other potentially simpler techniques have been proposed for quantification of breathing effort, and include ultrasound, electrical activity of the diaphragm (EA_{di}) and P_{aw}-derived parameters including the P_{aw} deflection during a short 100 ms occlusion at the start of inspiratory effort ($P_{0.1}$) or during a full breath occlusion (P_{occ}); for detailed descriptions and reference ranges, see Goligher *et al.* [61]. Ultrasound has become a well-established bedside tool for real-time visualisation of diaphragm contraction and movement, and to screen for respiratory muscle dysfunction [104]; however, diaphragm inspiratory thickening is unfortunately only weakly correlated to its pressure-generating capacity and not continuous [105, 106]. Advanced ultrasound techniques may better quantify muscle function and effort (*e.g.* strain imaging and shear wave elastography) and are a topic of future studies [104]. EA_{di} as measured *via* a dedicated naso-gastric catheter with electrodes reflects the

electrical activity of the crural diaphragm [107] and correlates reasonably well with breathing effort [108], but amplitudes are highly variable between subjects. EA_{di} could be particularly useful for identifying ventilated patients at risks for diaphragm disuse [109], to monitor within-patient changes in drive/effort or to assess patient–ventilator interaction. Notwithstanding, EA_{di} monitoring does not permit P_L estimation. Non-invasive parameters $P_{0.1}$ and P_{occ} can be measured with almost every intensive care unit (ICU) ventilator. Although $P_{0.1}$ was originally validated as a measure of respiratory drive [110], correlations with total inspiratory effort exist, but with large between-subject variations, and $P_{0.1}$ was found especially sensitive for detecting low effort [111], but also for detecting high effort with some ventilators [112] or to predict relapse of respiratory failure [113]. P_{occ} was recently validated in a small cohort as a measure to screen for high effort (P_{mus}) and excessive P_L [114]. Recent work demonstrated that $P_{0.1}$ and P_{occ} could also identify excessive P_L and the extremes of both low or high diaphragm effort specifically, with reasonable to excellent performance and with P_{occ} outperforming $P_{0.1}$ for detecting high ΔP_{di} [115]. Central venous pressure swings (ΔCVP) may directly reflect P_{pl} changes. ΔCVP was not a good predictor of ΔP_{oes} [116], but may identify excessive effort with reasonable accuracy in experimental work [117]; this needs clinical validation. Therefore, in patients under partially assisted mechanical ventilation, the aforementioned techniques may screen for potentially low or excessive efforts (or excessive P_L), but P_{oes} remains the reference standard for quantification.

Novel developments

P_{oes} integration into the ventilator monitor is now available for some machines and *in vivo* calibration methods [37] could potentially be automated, which improves the feasibility of P_{oes} monitoring at the bedside. This could also enable future integration of respiratory mechanics calculations and breathing effort monitoring directly into the ventilator, as well as applications of machine learning techniques for automated detection of low/excessive efforts, identification of asynchronies or recognition and removal of artefacts, for instance.

Whereas balloon catheters were introduced because P_{oes} monitoring with liquid or air-filled open catheters presented artefacts related to fluid menisci of surface tension effects (the balloon protected the catheter) [29], recently such catheters have been studied again but require further clinical validation [118–120]. Catheter-mounted microsensors measure P_{oes} directly inside the oesophagus, and thus have a faster frequency response compared with balloon catheters and are not subjected to signal dampening. This allows for more accurate recording of fast pressure changes [121], but may also result in larger cardiac or peristalsis artefacts that require adequate signal filtering. Although previous solid-state sensor techniques were mainly limited by large offsets and temperature drifts [120, 122], new technological advances may overcome these limitations.

Points for clinical practice

- P_{oes} monitoring allows partitioning of the lungs and the chest wall physiology during controlled ventilation. Tailoring ventilator settings based on the patient's individual respiratory physiology could offer additional solutions with mechanical ventilation to improve oxygenation, including optimisation of PEEP setting.
- P_{oes} monitoring allows measuring inspiratory effort and WOB, and assessing patient–ventilator interaction. This could facilitate providing lung- and diaphragm-protective ventilation during assisted ventilation and could optimise mechanical ventilation weaning.
- Technological advances allow P_{oes} monitoring to be implemented as part of routine respiratory monitoring in selected patients. This should stimulate the field to learn about the potential benefit of P_{oes} monitoring in the complex critically ill.
- Challenges and technical difficulties should be acknowledged before using P_{oes}-derived values to set the ventilator.

Questions for future research

- P_{oes} measurement could be a useful tool to optimise lung- and diaphragm-protective ventilation by adapting ventilator support levels to the patient's breathing effort. Future research should focus on defining the optimal range of breathing effort, especially upper limits for safe diaphragm effort, and the impact of targeting diaphragm effort on patient outcomes.
- Additional studies on the potential of P_{oes} monitoring to individualise PEEP settings are also needed.

Summary

There is a well-recognised need for optimising mechanical ventilation to protect the lungs and the diaphragm for each individual patient [6, 61]. Measurement of partitioned respiratory mechanics and quantification of lung stress and breathing effort using P_{oes} monitoring could improve our understanding of the patient's unique respiratory physiology and allows personalisation of mechanical ventilation settings under different conditions, as extensively discussed in this review. Although clinical evidence for P_{oes}-guided mechanical ventilation is yet limited and challenges remain, technological improvements have made P_{oes} monitoring feasible to become part of bedside respiratory monitoring in selected patients. This should encourage clinicians to develop new clinical studies aimed at identifying optimal and safe P_{oes}-guided targets for the management of the critically ill in order to improve ICU outcomes.

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References

1 Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; 342: 1301–1308.
2 Malhotra A. Low-tidal-volume ventilation in the acute respiratory distress syndrome. *N Engl J Med* 2007; 357: 1113–1120.
3 Papazian L, Aubron C, Brochard L, *et al.* Formal guidelines: management of acute respiratory distress syndrome. *Ann Intensive Care* 2019; 9: 69.
4 Fan E, Del Sorbo L, Goligher EC, *et al.* An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2017; 195: 1253–1263.
5 Ferguson ND, Fan E, Camporota L, *et al.* The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med* 2012; 38: 1573–1582.
6 Goligher EC, Dres M, Patel BK, *et al.* Lung- and diaphragm-protective ventilation. *Am J Respir Crit Care Med* 2020; 202: 950–961.
7 Grasso S, Terragni P, Birocco A, *et al.* ECMO criteria for influenza A (H1N1)-associated ARDS: role of transpulmonary pressure. *Intensive Care Med* 2012; 38: 395–403.
8 Bertoni M, Spadaro S, Goligher EC. Monitoring patient respiratory effort during mechanical ventilation: lung and diaphragm-protective ventilation. *Crit Care* 2020; 24: 106.
9 Jonkman AH, de Vries HJ, Heunks LMA. Physiology of the respiratory drive in ICU patients: implications for diagnosis and treatment. *Crit Care* 2020; 24: 104.
10 Spinelli E, Mauri T, Beitler JR, *et al.* Respiratory drive in the acute respiratory distress syndrome: pathophysiology, monitoring, and therapeutic interventions. *Intensive Care Med* 2020; 46: 606–618.
11 Dianti J, Fard S, Wong J, *et al.* Strategies for lung- and diaphragm-protective ventilation in acute hypoxemic respiratory failure: a physiological trial. *Crit Care* 2022; 26: 259.
12 Akoumianaki E, Maggiore SM, Valenza F, *et al.* The application of esophageal pressure measurement in patients with respiratory failure. *Am J Respir Crit Care Med* 2014; 189: 520–531.
13 Mauri T, Yoshida T, Bellani G, *et al.* Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives. *Intensive Care Med* 2016; 42: 1360–1373.
14 Cabello B, Mancebo J. Work of breathing. *Intensive Care Med* 2006; 32: 1311–1314.
15 Yoshida T, Brochard L. Esophageal pressure monitoring: why, when and how? *Curr Opin Crit Care* 2018; 24: 216–222.

16 Grieco DL, Chen L, Brochard L. Transpulmonary pressure: importance and limits. *Ann Transl Med* 2017; 5: 285.
17 Pham T, Telias I, Beitler JR. Esophageal manometry. *Respir Care* 2020; 65: 772–792.
18 Loring SH, Topulos GP, Hubmayr RD. Transpulmonary pressure: the importance of precise definitions and limiting assumptions. *Am J Respir Crit Care Med* 2016; 194: 1452–1457.
19 West JB. Respiratory Physiology – The Essentials. 9th Edn. Philadelphia, Lippincott Williams & Wilkins, 2011.
20 Agostini E, Mead J. Statics of the respiratory system. *In:* Fenn WO, Rahn H, eds. Handbook of Physiology: Respiration. Washington, American Physiological Society, 1964; pp. 387–409.
21 Cherniack RM, Fahri LE, Armstrong BW, *et al.* A comparison of esophageal and intrapleural pressure in man. *J Appl Physiol* 1955; 8: 203–211.
22 Talmor D, Sarge T, O'Donnell CR, *et al.* Esophageal and transpulmonary pressures in acute respiratory failure. *Crit Care Med* 2006; 34: 1389–1394.
23 Talmor D, Sarge T, Malhotra A, *et al.* Mechanical ventilation guided by esophageal pressure in acute lung injury. *N Engl J Med* 2008; 359: 2095–2104.
24 Gattinoni L, Chiumello D, Carlesso E, *et al.* Bench-to-bedside review: chest wall elastance in acute lung injury/acute respiratory distress syndrome patients. *Crit Care* 2004; 8: 350–355.
25 Staffieri F, Stripoli T, De Monte V, *et al.* Physiological effects of an open lung ventilatory strategy titrated on elastance-derived end-inspiratory transpulmonary pressure: study in a pig model. *Crit Care Med* 2012; 40: 2124–2131.
26 Yoshida T, Amato MBP, Grieco DL, *et al.* Esophageal manometry and regional transpulmonary pressure in lung injury. *Am J Respir Crit Care Med* 2018; 197: 1018–1026.
27 Bastia L, Engelberts D, Osada K, *et al.* Role of positive end-expiratory pressure and regional transpulmonary pressure in asymmetrical lung injury. *Am J Respir Crit Care Med* 2021; 203: 969–976.
28 Buytendijk HJ. Oesophagusdruk en longelasticiteit. [Esophageal Pressure and Lung Elasticity.] Groningen, Electrische Drukkerij I. Oppenheim, 1949.
29 Gibson GJ, Pride NB. Lung distensibility. The static pressure–volume curve of the lungs and its use in clinical assessment. *Br J Dis Chest* 1976; 70: 143–184.
30 Milic-Emili J, Mead J, Turner JM, *et al.* Improved technique for estimating pleural pressure from esophageal balloons. *J Appl Physiol* 1964; 19: 207–211.
31 Petit JM, Milic-Emili G. Measurement of endoesophageal pressure. *J Appl Physiol* 1958; 13: 481–485.
32 Fry DL, Stead WW, Ebert RV, *et al.* The measurement of intraesophageal pressure and its relationship to intrathoracic pressure. *J Lab Clin Med* 1952; 40: 664–673.
33 Mead J, McIlroy MB, Selverstone NJ, *et al.* Measurement of intraesophageal pressure. *J Appl Physiol* 1955; 7: 491–495.
34 Mojoli F, Chiumello D, Pozzi M, *et al.* Esophageal pressure measurements under different conditions of intrathoracic pressure. An *in vitro* study of second generation balloon catheters. *Minerva Anestesiol* 2015; 81: 855–864.
35 Baedorf Kassis E, Talmor D. Clinical application of esophageal manometry: how I do it. *Crit Care* 2021; 25: 6.
36 Mojoli F, Torriglia F, Orlando A, *et al.* Technical aspects of bedside respiratory monitoring of transpulmonary pressure. *Ann Transl Med* 2018; 6: 377.
37 Mojoli F, Iotti GA, Torriglia F, *et al. In vivo* calibration of esophageal pressure in the mechanically ventilated patient makes measurements reliable. *Crit Care* 2016; 20: 98.
38 Higgs BD, Behrakis PK, Bevan DR, *et al.* Measurement of pleural pressure with esophageal balloon in anesthesized humans. *Anesthesiology* 1983; 59: 340–343.
39 D'Angelo E, Robatto FM, Calderini E, *et al.* Pulmonary and chest wall mechanics in anesthetized paralyzed humans. *J Appl Physiol* 1991; 70: 2602–2610.
40 Lanteri CJ, Kano S, Sly PD. Validation of esophageal pressure occlusion test after paralysis. *Pediatr Pulmonol* 1994; 17: 56–62.
41 Cheng Y-P, Wu H-D, Jan G-J, *et al.* Removal of cardiac beat artifact in esophageal pressure measurement via a modified adaptive noise cancellation scheme. *Ann Biomed Eng* 2001; 29: 236–243.
42 Mukhopadhyay SK, Zara M, Telias I, *et al.* A singular spectrum analysis-based data-driven technique for the removal of cardiogenic oscillations in esophageal pressure signals. *IEEE J Transl Eng Health Med* 2020; 8: 3300211.
43 Beitler JR, Sarge T, Banner-Goodspeed VM, *et al.* Effect of titrating positive end-expiratory pressure (PEEP) with an esophageal pressure-guided strategy vs an empirical high PEEP-F_{IO_2} strategy on death and days free from mechanical ventilation among patients with acute respiratory distress syndrome: a randomized clinical trial. *JAMA* 2019; 321: 846–857.
44 Turbil E, Galerneau LM, Terzi N, *et al.* Positive-end expiratory pressure titration and transpulmonary pressure: the EPVENT 2 trial. *J Thorac Dis* 2019; 11: S2012–S2017.
45 Sarge T, Baedorf-Kassis E, Banner-Goodspeed V, *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: 1153–1163.

46 Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med* 2013; 369: 2126–2136.
47 Chiumello D, Carlesso E, Cadringher P, *et al.* Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2008; 178: 346–355.
48 Baedorf Kassis E, Loring SH, Talmor D. Mortality and pulmonary mechanics in relation to respiratory system and transpulmonary driving pressures in ARDS. *Intensive Care Med* 2016; 42: 1206–1213.
49 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; 100: 753–758.
50 Behazin N, Jones SB, Cohen RI, *et al.* Respiratory restriction and elevated pleural and esophageal pressures in morbid obesity. *J Appl Physiol* 2010; 108: 212–218.
51 Coudroy R, Vimpere D, Aissaoui N, *et al.* Prevalence of complete airway closure according to body mass index in acute respiratory distress syndrome. *Anesthesiology* 2020; 133: 867–878.
52 Chiumello D, Colombo A, Algieri I, *et al.* Effect of body mass index in acute respiratory distress syndrome. *Br J Anaesth* 2016; 116: 113–121.
53 De Jong A, Wrigge H, Hedenstierna G, *et al.* How to ventilate obese patients in the ICU. *Intensive Care Med* 2020; 46: 2423–2435.
54 Hibbert K, Rice M, Malhotra A. Obesity and ARDS. *Chest* 2012; 142: 785–790.
55 Pirrone M, Fisher D, Chipman D, *et al.* Recruitment maneuvers and positive end-expiratory pressure titration in morbidly obese ICU patients. *Crit Care Med* 2016; 44: 300–307.
56 Fumagalli J, Berra L, Zhang C, *et al.* Transpulmonary pressure describes lung morphology during decremental positive end-expiratory pressure trials in obesity. *Crit Care Med* 2017; 45: 1374–1381.
57 De Santis Santiago R, Teggia Droghi M, Fumagalli J, *et al.* High pleural pressure prevents alveolar overdistension and hemodynamic collapse in acute respiratory distress syndrome with class III obesity. A clinical trial. *Am J Respir Crit Care Med* 2021; 203: 575–584.
58 Liou J, Doherty D, Gillin T, *et al.* Retrospective review of transpulmonary pressure guided positive end-expiratory pressure titration for mechanical ventilation in class II and III obesity. *Crit Care Explor* 2022; 4: e0690.
59 Rowley DD, Arrington SR, Enfield KB, *et al.* Transpulmonary pressure-guided lung-protective ventilation improves pulmonary mechanics and oxygenation among obese subjects on mechanical ventilation. *Respir Care* 2021; 66: 1049–1058.
60 Florio G, Ferrari M, Bittner EA, *et al.* A lung rescue team improves survival in obesity with acute respiratory distress syndrome. *Crit Care* 2020; 24: 4.
61 Goligher EC, Jonkman AH, Dianti J, *et al.* Clinical strategies for implementing lung and diaphragm-protective ventilation: avoiding insufficient and excessive effort. *Intensive Care Med* 2020; 46: 2314–2326.
62 Levine S, Budak MT, Sonnad S, *et al.* Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. *N Engl J Med* 2008; 358: 1327–1335.
63 Goligher EC, Fan E, Herridge MS, *et al.* Evolution of diaphragm thickness during mechanical ventilation. Impact of inspiratory effort. *Am J Respir Crit Care Med* 2015; 192: 1080–1088.
64 Hooijman PE, Beishuizen A, Witt CC, *et al.* Diaphragm muscle fiber weakness and ubiquitin–proteasome activation in critically ill patients. *Am J Respir Crit Care Med* 2015; 191: 1126–1138.
65 van den Berg M, Hooijman PE, Beishuizen A, *et al.* Diaphragm atrophy and weakness in the absence of mitochondrial dysfunction in the critically ill. *Am J Respir Crit Care Med* 2017; 196: 1544–1558.
66 Orozco-Levi M, Lloreta J, Minguella J, *et al.* Injury of the human diaphragm associated with exertion and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001; 164: 1734–1739.
67 Ebihara S, Hussain SNA, Danialou G, *et al.* Mechanical ventilation protects against diaphragm injury in sepsis: interaction of oxidative and mechanical stresses. *Am J Respir Crit Care Med* 2002; 165: 221–228.
68 Zhu E, Petrof BJ, Gea J, *et al.* Diaphragm muscle fiber injury after inspiratory resistive breathing. *Am J Respir Crit Care Med* 1997; 155: 1110–1116.
69 Damiani LF, Engelberts D, Bastia L, *et al.* Impact of reverse triggering dyssynchrony during lung-protective ventilation on diaphragm function: an experimental model. *Am J Respir Crit Care Med* 2022; 205: 663–673.
70 de Vries HJ, Jonkman AH, de Grooth HJ, *et al.* Lung- and diaphragm-protective ventilation by titrating inspiratory support to diaphragm effort. *Crit Care Med* 2022; 50: 192–203.
71 Parthasarathy S, Jubran A, Laghi F, *et al.* Sternomastoid, rib cage, and expiratory muscle activity during weaning failure. *J Appl Physiol* 2007; 103: 140–147.
72 Lessard MR, Lofaso F, Brochard L. Expiratory muscle activity increases intrinsic positive end-expiratory pressure independently of dynamic hyperinflation in mechanically ventilated patients. *Am J Respir Crit Care Med* 1995; 151: 562–569.
73 Doorduin J, Roesthuis LH, Jansen D, *et al.* Respiratory muscle effort during expiration in successful and failed weaning from mechanical ventilation. *Anesthesiology* 2018; 129: 490–501.
74 Shi Z-H, Jonkman A, de Vries H, *et al.* Expiratory muscle dysfunction in critically ill patients: towards improved understanding. *Intensive Care Med* 2019; 45: 1061–1071.
75 Mead J, Loring SJ. Volume displacements of the chest wall and their mechanical significance. *In:* Roussos C, Macklem PT, eds. The Thorax: Part A. New York, Dekker, 1985; pp. 369–392.

76 American Thoracic Society/European Respiratory Society. ATS/ERS statement on respiratory muscle testing. *Am J Respir Crit Care Med* 2002; 166: 518–624.

77 Collett PW, Perry C, Engel LA. Pressure-time product, flow, and oxygen cost of resistive breathing in humans. *J Appl Physiol* 1985; 58: 1263–1272.

78 de Vries H, Jonkman A, Shi Z-H, *et al.* Assessing breathing effort in mechanical ventilation: physiology and clinical implications. *Ann Transl Med* 2018; 6: 387.

79 Yoshida T, Fujino Y, Amato MBP, *et al.* Fifty years of research in ARDS. Spontaneous breathing during mechanical ventilation. Risks, mechanisms, and management. *Am J Respir Crit Care Med* 2017; 195: 985–992.

80 Morais CCA, Koyama Y, Yoshida T, *et al.* High positive end-expiratory pressure renders spontaneous effort noninjurious. *Am J Respir Crit Care Med* 2018; 197: 1285–1296.

81 Yoshida T, Nakahashi S, Nakamura MAM, *et al.* Volume-controlled ventilation does not prevent injurious inflation during spontaneous effort. *Am J Respir Crit Care Med* 2017; 196: 590–601.

82 Yoshida T, Torsani V, Gomes S, *et al.* Spontaneous effort causes occult pendelluft during mechanical ventilation. *Am J Respir Crit Care Med* 2013; 188: 1420–1427.

83 Yoshida T, Uchiyama A, Matsuura N, *et al.* The comparison of spontaneous breathing and muscle paralysis in two different severities of experimental lung injury. *Crit Care Med* 2013; 41: 536–545.

84 Wrigge H, Zinserling J, Neumann P, *et al.* Spontaneous breathing improves lung aeration in oleic acid-induced lung injury. *Anesthesiology* 2003; 99: 376–384.

85 Bianchi I, Grassi A, Pham TI, *et al.* Reliability of plateau pressure during patient-triggered assisted ventilation. Analysis of a multicentre database. *J Crit Care* 2022; 68: 96–103.

86 Yoshida T, Amato MBP, Kavanagh BP. Understanding spontaneous vs. ventilator breaths: impact and monitoring. *Intensive Care Med* 2018; 44: 2235–2238.

87 Blanch L, Villagra A, Sales B, *et al.* Asynchronies during mechanical ventilation are associated with mortality. *Intensive Care Med* 2015; 41: 633–641.

88 de Wit M, Miller KB, Green DA, *et al.* Ineffective triggering predicts increased duration of mechanical ventilation. *Crit Care Med* 2009; 37: 2740–2745.

89 Kyo M, Shimatani T, Hosokawa K, *et al.* Patient–ventilator asynchrony, impact on clinical outcomes and effectiveness of interventions: a systematic review and meta-analysis. *J Intensive Care* 2021; 9: 50.

90 Kondili E, Xirouchaki N, Georgopoulos D. Modulation and treatment of patient–ventilator dyssynchrony. *Curr Opin Crit Care* 2007; 13: 84–89.

91 Colombo D, Cammarota G, Alemani M, *et al.* Efficacy of ventilator waveforms observation in detecting patient–ventilator asynchrony. *Crit Care Med* 2011; 39: 2452–2457.

92 Jonkman AH, Holleboom MC, de Vries HJ, *et al.* Expiratory muscle relaxation-induced ventilator triggering. *Chest* 2022; 161: e337–e341.

93 Pham T, Montanya J, Telias I, *et al.* Automated detection and quantification of reverse triggering effort under mechanical ventilation. *Crit Care* 2021; 25: 60.

94 Blanch L, Sales B, Montanya J, *et al.* Validation of the Better Care system to detect ineffective efforts during expiration in mechanically ventilated patients: a pilot study. *Intensive Care Med* 2012; 38: 772–780.

95 Mulqueeny Q, Ceriana P, Carlucci A, *et al.* Automatic detection of ineffective triggering and double triggering during mechanical ventilation. *Intensive Care Med* 2007; 33: 2014–2018.

96 Sottile PD, Albers D, Higgins C, *et al.* The association between ventilator dyssynchrony, delivered tidal volume, and sedation using a novel automated ventilator dyssynchrony detection algorithm. *Crit Care Med* 2018; 46: e151–e157.

97 Rodriguez PO, Tiribelli N, Gogniat E, *et al.* Automatic detection of reverse-triggering related asynchronies during mechanical ventilation in ARDS patients using flow and pressure signals. *J Clin Monit Comput* 2020; 34: 1239–1246.

98 Thille AW, Harrois A, Schortgen F, *et al.* Outcomes of extubation failure in medical intensive care unit patients. *Crit Care Med* 2011; 39: 2612–2618.

99 Vallverdú I, Calaf N, Subirana M, *et al.* Clinical characteristics, respiratory functional parameters, and outcome of a two-hour T-piece trial in patients weaning from mechanical ventilation. *Am J Respir Crit Care Med* 1998; 158: 1855–1862.

100 Béduneau G, Pham T, Schortgen F, *et al.* Epidemiology of weaning outcome according to a new definition. The WIND study. *Am J Respir Crit Care Med* 2017; 195: 772–783.

101 Jubran A, Tobin MJ. Pathophysiologic basis of acute respiratory distress in patients who fail a trial of weaning from mechanical ventilation. *Am J Respir Crit Care Med* 1997; 155: 906–915.

102 Proctor HJ, Woolson R. Prediction of respiratory muscle fatigue by measurements of the work of breathing. *Surg Gynecol Obstet* 1973; 136: 367–370.

103 Jubran A, Grant BJB, Laghi F, *et al.* Weaning prediction: esophageal pressure monitoring complements readiness testing. *Am J Respir Crit Care Med* 2005; 171: 1252–1259.

104 Tuinman PR, Jonkman AH, Dres M, *et al.* Respiratory muscle ultrasonography: methodology, basic and advanced principles and clinical applications in ICU and ED patients – a narrative review. *Intensive Care Med* 2020; 46: 594–605.

105 Poulard T, Bachasson D, Fossé Q, *et al.* Poor correlation between diaphragm thickening fraction and transdiaphragmatic pressure in mechanically ventilated patients and healthy subjects. *Anesthesiology* 2022; 136: 162–175.

106 Oppersma E, Hatam N, Doorduin J, *et al.* Functional assessment of the diaphragm by speckle tracking ultrasound during inspiratory loading. *J Appl Physiol* 2017; 123: 1063–1070.

107 Sinderby C, Navalesi P, Beck J, *et al.* Neural control of mechanical ventilation in respiratory failure. *Nat Med* 1999; 5: 1433–1436.

108 Piquilloud L, Beloncle F, Richard J-CM, *et al.* Information conveyed by electrical diaphragmatic activity during unstressed, stressed and assisted spontaneous breathing: a physiological study. *Ann Intensive Care* 2019; 9: 89.

109 Sklar MC, Madotto F, Jonkman A, *et al.* Duration of diaphragmatic inactivity after endotracheal intubation of critically ill patients. *Crit Care* 2021; 25: 26.

110 Whitelaw WA, Derenne JP, Milic-Emili J. Occlusion pressure as a measure of respiratory center output in conscious man. *Respir Physiol* 1975; 23: 181–199.

111 Telias I, Junhasavasdikul D, Rittayamai N, *et al.* Airway occlusion pressure as an estimate of respiratory drive and inspiratory effort during assisted ventilation. *Am J Respir Crit Care Med* 2020; 201: 1086–1098.

112 Beloncle F, Piquilloud L, Olivier P-Y, *et al.* Accuracy of $P_{0.1}$ measurements performed by ICU ventilators: a bench study. *Ann Intensive Care* 2019; 9: 104.

113 Esnault P, Cardinale M, Hraiech S, *et al.* High respiratory drive and excessive respiratory efforts predict relapse of respiratory failure in critically ill patients with COVID-19. *Am J Respir Crit Care Med* 2020; 202: 1173–1178.

114 Bertoni M, Telias I, Urner M, *et al.* A novel non-invasive method to detect excessively high respiratory effort and dynamic transpulmonary driving pressure during mechanical ventilation. *Crit Care* 2019; 23: 346.

115 de Vries HJ, Tuinman PR, Jonkman AH, *et al.* Performance of noninvasive airway occlusion maneuvers to assess lung stress and diaphragm effort in mechanically ventilated critically ill patients. *Anesthesiology* 2022; 138: 274–288.

116 Bellemare P, Goldberg P, Magder SA. Variations in pulmonary artery occlusion pressure to estimate changes in pleural pressure. *Intensive Care Med* 2007; 33: 2004–2008.

117 Colombo J, Spinelli E, Grasselli G, *et al.* Detection of strong inspiratory efforts from the analysis of central venous pressure swings: a preliminary clinical study. *Minerva Anestesiol* 2020; 86: 1296–1304.

118 Verscheure S, Massion PB, Gottfried S, *et al.* Measurement of pleural pressure swings with a fluid-filled esophageal catheter vs pulmonary artery occlusion pressure. *J Crit Care* 2017; 37: 65–71.

119 Massion PB, Berg J, Samalea Suarez N, *et al.* Novel method of transpulmonary pressure measurement with an air-filled esophageal catheter. *Intensive Care Med Exp* 2021; 9: 47.

120 Augusto RM, Albuquerque ALP, Jaeger T, *et al.* Stability and agreement of a microtransducer and an air-filled balloon esophageal catheter in the monitoring of esophageal pressure. *Respir Care* 2017; 62: 215–221.

121 MacAskill W, Hoffman B, Johnson MA, *et al.* Pressure measurement characteristics of a micro-transducer and balloon catheters. *Physiol Rep* 2021; 9: e14831.

122 Peters RJ, Meijer JH, Kingma R, *et al.* Evaluation of catheter-mounted transducers for intra-oesophageal pressure recording in respiratory function tests. *Med Biol Eng Comput* 1998; 36: 562–567.