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REVIEW

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Assessing inspiratory drive and effort in critically ill patients at the bedside

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Abstract

Monitoring inspiratory drive and effort may aid proper selection and setting of respiratory support in patients with acute respiratory failure (ARF), whether they are intubated or not. Although diaphragmatic electrical activity (EAdi) and esophageal manometry can be considered the reference methods for assessing respiratory drive and inspiratory effort, respectively, various alternative techniques exist, each with distinct advantages and limitations. This narrative review provides a comprehensive overview of bedside methods to assess respiratory drive and effort, with a primary focus on patients with ARF. First, EAdi and esophageal manometry are described and discussed as reference techniques. Then, alternative methods are categorized along the neuromechanical pathway from inspiratory drive to muscular effort into three groups: (1) techniques assessing the respiratory drive: airway occlusion pressure (P0.1), mean inspiratory flow (Vt/Ti) and respiratory muscle surface electromyography (sEMG); (2) techniques assessing the respiratory muscle effort: whole-breath occlusion pressure (ΔPocc), pressure-muscle index (PMI), nasal pressure swing (ΔPnose), diaphragm ultrasonography (USdi), central venous pressure swing (ΔCVP), breathing effort (BREF) models, and flow index; (3) techniques and clinical parameters assessing the consequences of effort: tidal volume (Vt), electrical impedance tomography (EIT), dyspnea. For each, we summarize the physiological rationale, measurement methodology, interpretation of results, and key limitations.

Keywords Inspiratory effort, Respiratory monitoring, Patient self-inflicted lung injury, Esophageal pressure, Acute respiratory failure, Ventilator-induced diaphragm dysfunction.

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Background and rationale

The current approach to ventilatory support in acute respiratory failure (ARF) favors maintaining a degree of spontaneous breathing, based on the rationale that it may improve gas exchange, promote more physiological lung aeration, and help preserve respiratory muscle function [1–4]. Further, the growing use of non-invasive respiratory support (i.e., high-flow nasal cannula [HFNC] and non-invasive mechanical ventilation [NIV]), accelerated by the COVID-19 pandemic, has broadened ARF management outside the intensive care unit (ICU) [5–7]. Preserving spontaneous breathing could help maintain respiratory muscle function and reduce complications associated with mechanical ventilation (MV) [2, 4, 8]. However, this strategy also carries potential risks, especially if respiratory effort becomes excessive [9, 10]. Intense inspiratory effort can indeed generate very negative intrathoracic pressures, potentially leading to negative alveolar pressure, high transpulmonary pressures with large tidal volume (Vt), increased left ventricular afterload, and the development of pulmonary edema [11]. These mechanisms may deteriorate lung mechanics and contribute to patient self-inflicted lung injury (P-SILI), ultimately worsening clinical outcomes [12–15]. Thus, there is a sound physiological rationale for assessing drive and effort in patients with ARF to enable prompt corrective actions (i.e., pharmacologic sedation/de-sedation or MV escalation/de-escalation [16]). While diaphragmatic electrical activity (EAdi) and esophageal manometry can be considered the reference techniques for quantifying inspiratory drive and effort respectively [17], various alternative assessment methods with different potential for bedside use have been investigated [18–20].

This narrative review presents current bedside methods for assessing inspiratory drive and effort, beginning with the introduction of EAdi and esophageal manometry as reference standards. Subsequently, alternative techniques are presented and classified according to the neuro-ventilatory cascade: (1) methods for assessing the inspiratory drive, (2) methods for assessing the inspiratory muscle effort, and (3) methods for evaluating the consequences of effort. For each technique, we provide a summary of the physiological rationale, measurement methodology, clinical interpretation, and key limitations. Importantly, the techniques described in this review differ substantially in terms of how extensively they have been investigated and adopted in clinical practice. Some methods have been the focus of multiple physiological and clinical studies and are routinely used at the bedside, whereas others are more recent, with limited available data and lower uptake in daily care. These differences are highlighted throughout the review and summarized in the final section.

Inspiratory drive and effort: pathophysiology, clinical relevance and reference methods for assessment

Pathophysiology

Respiratory drive refers to the oscillatory neural output generated by the brainstem respiratory centers. It primarily originates from the preBötzinger complex, which plays a central role in initiating inspiration, and is shaped by modulatory structures such as the Bötzinger complex and retrotrapezoid nucleus, which contribute to pattern formation and chemosensory integration [21, 22]. This output mainly relies on feedback from peripheral and central chemoreceptors (sensing arterial and cerebrospinal fluid pH and gas tension) [23], irritant receptors in the lung and chest wall, and cortical feedback [15, 22]. Respiratory drive determines primarily the intensity, and only secondarily the frequency, of the impulses delivered to the respiratory pump and represents the initiating signal for ventilation. This is consistent with experimental evidence showing that in response to chemoreceptor stimulation (e.g., hypercapnia), the motor output is primarily regulated by changes in intensity rather than in frequency, making respiratory rate a less sensitive indicator of drive [24]. Inspiratory effort refers to the pressure generated by the respiratory muscles—primarily the diaphragm—in response to the neural command, commonly expressed as respiratory muscle pressure (Pmus) [15]. The contraction and downward displacement of the diaphragm result in the expansion of the thoracic cage, which decreases pleural and alveolar pressures, thereby driving lung inflation. In patients with ARF, altered gas exchange and respiratory mechanics, inflammation, and emotional factors variably contribute to increasing respiratory drive and effort. When the load imposed on the diaphragm rises, other muscles are recruited to assist inspiration, including sternocleidomastoid, parasternal, scalene and intercostal muscles. Notably, some of these—such as the scalene and intercostal muscles—are not merely accessory but contribute to normal inspiration. In more severe cases, even expiratory muscles may be activated to enhance inspiratory muscle capacity [25].

Normally, inspiratory drive and effort are coupled: when the drive increases, there is a parallel increase in muscle activation and mechanical output. However, in critically ill patients, this neuromechanical coupling can become disrupted, as the relationship between respiratory drive and effort varies considerably depending on respiratory muscle strength and respiratory system mechanics. As a result, relying solely on effort may lead to underestimating disease severity, which a disproportionately high drive could instead indicate. Conversely, monitoring only the respiratory drive may fail to detect harmful inspiratory effort, particularly in the most critically ill patients. This possible dissociation between drive

and effort is not only a monitoring challenge, but rather a key mechanism of dyspnea. When neural drive increases but fails to produce sufficient mechanical output—due to respiratory muscle weakness, impaired compliance, or under-assistance—a mismatch arises between intended and actual ventilation. This neuromechanical uncoupling triggers respiratory-related brain suffering, of which dyspnea is the conscious manifestation [26]. Importantly, this mismatch can occur even in the absence of overt physiological abnormalities, contributing to the under-recognition of distress in patients with ARF.

Clinical relevance

The importance of preserving inspiratory drive and effort during MV and non-invasive respiratory support has been increasingly recognized [27–31]. Maintaining a certain degree of diaphragmatic activity may improve gas exchange and lung aeration, particularly through the recruitment of dorsal lung regions [32, 33]. Notably, respiratory support—invasive or non-invasive—interacts substantially with spontaneous breathing; however, its clinical effects are complex, often bidirectional, and vary considerably among patients.

Inspiratory support generally unloads the respiratory muscles and potentially decreases drive and effort [34–36]. However, if the level of assistance is lower than the patient's ventilatory demand, not properly synchronized with the patient's effort, or poorly tolerated—such as in cases of delayed triggering, an excessive backup rate, or discomfort from the interface—respiratory drive may increase. This heightened drive can lead to stronger inspiratory efforts, dyspnea, and patient–ventilator asynchrony. Positive end-expiratory pressure (PEEP) may decrease inspiratory drive and effort mainly by improving lung compliance. However, it may also have the opposite effect if it induces overdistension or hemodynamic compromise. Additionally, PEEP and the level of assistance may influence neuromechanical coupling, potentially impairing diaphragmatic efficiency and, in turn, altering inspiratory effort and its alignment with neural drive [37–40].

Understanding how support settings influence the drive–effort relationship seems critical, as mismatches between neural demand and mechanical assistance can lead to clinically relevant patterns such as over-assistance or under-assistance. Over-assistance occurs when mechanical support surpasses neural demand, resulting in minimal inspiratory effort and risks such as diaphragm weakness. This can lead to prolonged ICU stays and cognitive impairment [27, 41–45]. Clinically, it may present as bradypnea and large thoracic expansion, with ventilator waveforms showing no inspiratory deflection and late cycling (i.e., the ventilator cycles well after the patient stops actively inspiring). Such excessive unloading can lead to diaphragm disuse atrophy [31, 46–48], causing dyspnea even after ICU discharge [49]. Excessive inspiratory efforts can also be detrimental. This typically occurs when the level of assistance fails to meet the patient's respiratory demand—i.e., under-assistance—leading to persistently elevated inspiratory drive and a marked increase in respiratory muscular effort. Clinically, this may present as tachypnea, nasal flaring, and visible use of accessory muscles. On ventilator waveforms, under-assistance is usually associated with scooped pressure-time curves during volume-controlled mode. This pattern reflects patient inspiratory effort occurring despite fixed inspiratory flow, and may be accompanied by early cycling (i.e., the ventilator cycles before the patient finishes actively inspiring). When the neural inspiratory time exceeds the ventilator-set inspiratory time, this mismatch can deform the pressure plateau and, in some cases, lead to double triggering [50].

When inspiratory effort becomes higher than normal, a substantial portion of cardiac output is diverted to the respiratory muscles [51, 52]. While normally accounting for 5–10% of total oxygen consumption, the oxygen cost of breathing can surge to 50% in critically ill patients, further impairing oxygen delivery in shock states [53, 54]. Moreover, inspiratory efforts exceeding physiological limits may trigger P-SILI [55] especially when the underlying injury is more severe [13, 56, 57] as they cause both alveolar overdistension and cyclic recruitment of collapsed lung areas [13, 55]. These injurious patterns are driven by increased transpulmonary pressure resulting from a marked decrease in pleural pressure during patient-triggered inspiration, leading to excessive lung stress—often exceeding the normal maximal values observed at total lung capacity in healthy individuals (≈ 30 cmH_2O) [58, 59]. The vascular components of this injury may also be significant. The resulting deterioration in gas exchange and respiratory mechanics, in turn, further increases respiratory drive in a vicious cycle, exposing the lungs to the risk of even stronger inspiratory efforts [55]. A U-shaped relationship between inspiratory effort and the risk of diaphragm or lung injury could then be hypothesized, where the extremes of effort– either insufficient or excessive–may contribute to damage [60, 61].

Finally, maintaining adequate inspiratory drive and effort appears important not only to achieve a balanced level of patient–ventilator interaction, but also to improve its quality. Dyssynchronous unloading, as seen in reverse triggering and ineffective efforts, can result in prolonged diaphragm activation and induce eccentric contractions. This abnormal activity can overstretch muscle fibers, potentially resulting in microtrauma and long-term diaphragm weakness [62]. Asynchronies could also cause lung injury, especially when resulting in exposure to high

Vt, for instance, with breath stacking [63]. These considerations all underscore the importance of assessing drive and effort to optimize respiratory management in critically ill patients with ARF.

Reference method for assessing the inspiratory drive: diaphragm electrical activity

In humans, the intensity of output from the respiratory center cannot be measured directly. Instead, it can be estimated through various downstream effects, including the EAdi. The EAdi can be measured via a nasogastric catheter embedded with ring-shaped electrodes that are positioned at the level of the crural diaphragm [64]. This catheter was originally designed to control the ventilator timing and pressurization to enhance patient-ventilator interaction (with Neurally Adjusted Ventilatory Assist) [65] but it can also be used with other ventilator modes and in non-intubated patients.EAdi captures the electrical signal originating from the crural part of the diaphragm. As long as the phrenic nerves and neuromuscular junctions are intact, and extra-diaphragmatic muscles are not significantly activated, EAdi and other related measurements, such as the average rate of increase of EAdi (EAdi/dt), serve as the most precise accessible proxy for respiratory drive [66]. The measurement is not widely available since it requires specialized equipment. Correct catheter placement and processing of the signal are facilitated by ventilator software. Cardiac artifacts may occur, especially when the drive is low (and the signal-to-noise ratio is low). However, these artifacts are typically removed through filtering or signal processing algorithms. The measurement is somewhat invasive, especially for non-intubated patients, but no more than placing a standard nasogastric feeding tube. Typical peak EAdi values are 10–20 μV in non-intubated healthy volunteers [67] and 5–20 μV in mechanically ventilated patients [20]. The signal remains stable with different lung volumes [68] and in individual patients, changes in EAdi closely correlate with changes in dynamic transpulmonary pressure ($\Delta Plung_{dyn}$) or esophageal pressure swings (ΔPes) [69, 70]. However, the same EAdi can be associated with very different ΔPes (or $\Delta Plung_{dyn}$) in different patients [71, 72]. Individual changes in EAdi (e.g. evolving over time, or after adjustment of sedation or ventilator support) therefore provide more information than single static measurements. Normalization of EAdi to maximum EAdi has been proposed [73] but obtaining maximal volitional inspiratory efforts in critically ill patients is often unfeasible. Alternatively, EAdi can be used to estimate effort (and not only drive) via a conversion factor that is obtained during an end-expiratory occlusion maneuver. In this context, the neuromuscular efficiency (NME) index is calculated as the ratio between the maximal negative airway pressure deflection and the corresponding EAdi amplitude during the occlusion (in $cmH_2O/\mu V$). This conversion factor can then be used to estimate ΔPes from tidal EAdi amplitudes [71]. Values < 5 or > 10 cmH_2O of ΔPes estimated in this way may be considered too low or too high [72, 74, 75]. Of note, changes in NME may reflect accessory muscle recruitment, which is not captured by EAdi and contributes to the index's high variability in clinical practice [72, 76]. EAdi specifically reflects neuronal output to the diaphragm or "diaphragm respiratory drive". In cases of ventilator-induced diaphragmatic dysfunction or phrenic nerve injury, and similar to intense exercise in healthy subjects [77], neuronal output to other inspiratory and expiratory muscles may be significant but is not recorded by EAdi. In ICU patients the contribution of the diaphragm is very often substantially less than in healthy subjects and it is not clear how EAdi will reflect the total drive. In such instances, the rate of increase in Pmus (Pmus/dt), generated by all respiratory muscles and measured using esophageal manometry, may provide a more accurate representation of overall respiratory drive, but only if neural transmission and muscle pressure generation remain intact.

Reference method for assessing the inspiratory effort: esophageal manometry

The esophagus, lacking structural rigidity, passively transmits intrathoracic pressure changes, making ΔPes a close approximation of pleural pressure swings generated by the respiratory muscles [17]. Esophageal manometry thus represents the reference method for assessing the inspiratory effort: the greater the ΔPes, the stronger the inspiratory effort. The method typically requires a nasogastric catheter with a thin-wall latex balloon or solid-state sensor, which can be integrated into feeding tubes to reduce invasiveness and cost [74]. Notably, esophageal pressure can also be measured using balloon-less catheters, which have shown reliable performance in both experimental and clinical settings [78, 79]. Correct balloon positioning in the mid-esophagus ensures reliable Pes signals. In intubated and non-intubated patients, positioning can be verified by the presence of cardiac artifacts on the pressure waveform and by radiopaque markers on the chest radiograph. Calibration can be manual or semi-automated via ventilator systems [80]. In intubated patients, proper filling volume and pressure transmission can (and should) be confirmed by an occlusion test [81] aiming for a ΔPes/ΔPaw ratio between 0.8 and 1.2 [17]. In non-intubated patients with ARF, the occlusion test via a mouthpiece is often unfeasible and may yield inaccurate results due to upper airway compliance and pressure dissipation. Airway closure and the presence of an airway opening pressure can further compromise measurement accuracy [82].

Esophageal manometry also provides multiple derived measures of increasing complexity and accuracy. Using of a double-balloon catheter enables simultaneous measurement of gastric pressure (Pga), allowing for the assessment of the transdiaphragmatic pressure (Pdi = Pga - Pes). (eFigure 1,Supplement). ΔPes as an index of inspiratory effort does not account for time; multiplying it by respiratory rate (RR; i.e., pressure-rate product) can complement static measurements [83]. To better account for effort duration and volume displacement, ΔPes can be further refined to derive the pressure-time product (PTP), which quantifies the difference between ΔPes over inspiratory time and the work of breathing (WOB), which integrates ΔPes and Vt. These other measurements also require knowledge of Ecw. While both provide a better estimate of the oxygen cost of breathing, their bedside use is limited by complexity [84, 85].

Beyond ΔPes, Pmus provides a physiologically integrated estimate of inspiratory effort, capturing the global pressure generated by the respiratory muscles while also accounting for the elastic and resistive load of the chest wall. At any point during inspiration, Pmus can be defined as the difference between the pleural pressure that would occur in the absence of respiratory muscle activity (Ppl, passive) and the actual pleural pressure (Ppl, actual, approximated by Pes):

$$Pmus = Ppl, passive - Ppl, actual$$
$$= (Ecw \times V) + (Rcw \times Flow) + Ppl_{FRC} - Pes$$

where Ecw and Rcw are the elastance and resistance of the chest wall, V is the inspired volume above passive functional residual capacity (FRC), Flow is the inspiratory flow, and Ppl_{FRC} reflects the passive pleural pressure

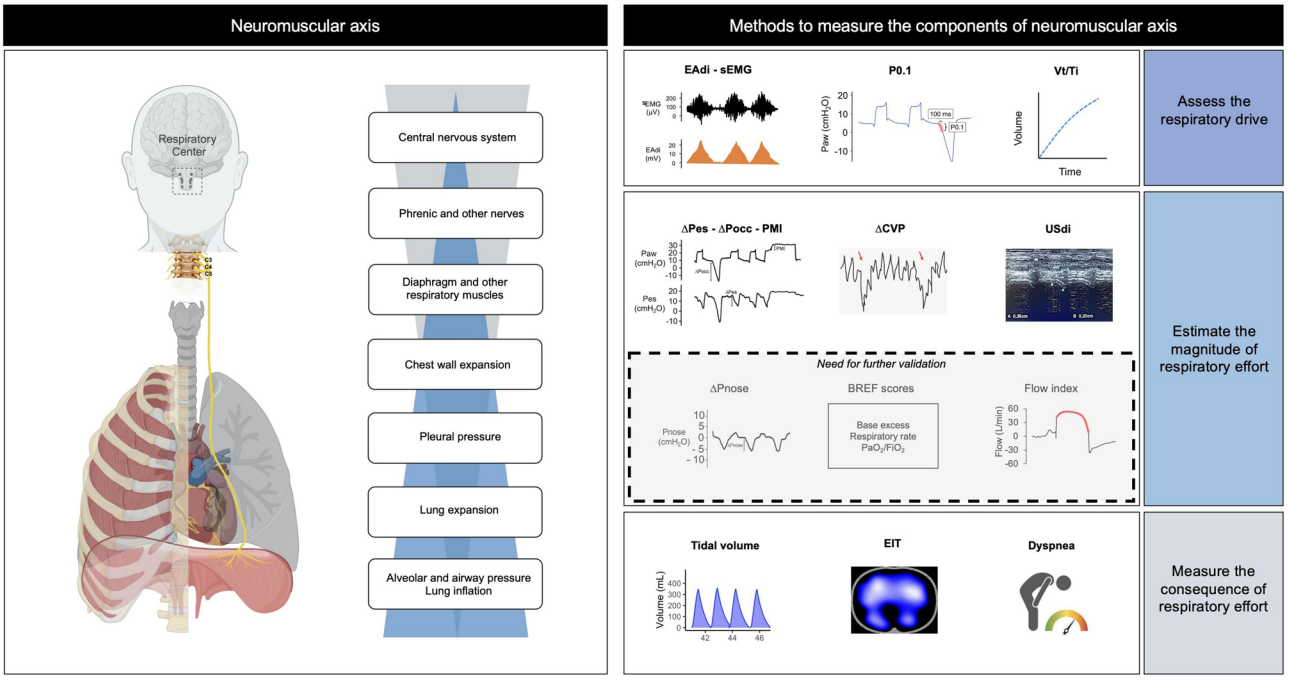

Fig. 1 Techniques for bedside assessment of inspiratory drive and effort along the respiratory drive cascade. Left panel. *Integrative framework linking respiratory drive and the neuromuscular axis*. Transforming the central respiratory drive into effective inspiratory effort involves multiple hierarchical steps (blue pyramid). The impulse to breathe originates in the respiratory centers of the brainstem and is transmitted via the phrenic nerves to the neuromuscular junction. The activation of the respiratory muscles expands the chest wall, progressively lowering pleural pressure and expanding the lungs. As a result, alveolar and airway pressures decrease, creating a gradient relative to atmospheric pressure that drives gas into the respiratory system. As these descending processes unfold, ascending feedback mechanisms (gray pyramid) are simultaneously activated at each level. These inputs continuously relay information to the respiratory centers, enabling dynamic control of breathing. The respiratory effort can be assessed at various points along the neuromuscular axis. Right panel. *Principal techniques to estimate inspiratory drive and effort at the bedside.* Techniques are organized along the respiratory drive cascade and categorized according to their physiological relationship with inspiratory effort: methods assessing the respiratory drive (e.g., EAdi, P0.1, mean inspiratory flow, respiratory muscle surface EMG); methods assessing the respiratory muscle effort (e.g., ΔPes, ΔPocc, PMI, ΔPnose, USdi, ΔCVP, BREF models, and flow index); and methods evaluating the consequences of effort (e.g., tidal volume, electrical impedance tomography, dyspnea perception). Importantly, these techniques differ substantially in terms of validation status, clinical uptake, and supporting evidence. While methods such as P0.1, ΔPocc, USdi, and ΔCVP have been extensively studied and are widely adopted in both physiological research and clinical practice, others—such as ΔPnose, the flow index, and the BREF models —are promising but remain in earlier stages of development and require further clinical validation before broader implementation.ΔPes, esophageal pressure swing; ΔPocc, whole-breath occlusion pressure; P0.1, airway occlusion pressure; PMI, pressure-muscle-index; ΔPnose, nasal pressure swing; sEMG, (respiratory muscle) surface electromyography; EAdi electrical activity of the diaphragm; USdi, diaphragm ultrasonography; ΔCVP, central venous pressure swing; Vt, tidal volume; Ti, inspiratory time; EIT, electrical impedance tomography

at FRC (often assumed as baseline Pes at end-expiration under relaxed conditions).

In clinical practice, this comprehensive formulation is often simplified as:

$$Pmus \approx (Ecw \times Vt) - \Delta Pes$$

assuming no expiratory muscle activity, negligible chest wall resistance, and stable end-expiratory pleural pressure. However, such assumptions may not hold, particularly in patients exhibiting active expiration—a condition frequently observed during assisted ventilation. Additionally, Rcw may become relevant at high inspiratory flows. Consequently, absolute values of Pmus should be interpreted with caution, while Pmus swings across breaths may still offer reliable insight into changes in inspiratory effort, as long as estimation biases remain constant within the same patient. Notably, the precise measurement of Pmus is further complicated by the interplay between expiratory and inspiratory muscle activity. This interplay explains, for instance, that part of the initial decay in esophageal pressure may be simply due to the relaxation of the expiratory muscles, as evidenced by Pga swings [86].

There is still no consensus on the definition of the injurious inspiratory effort threshold [63]. In healthy individuals, ΔPes is typically only a few cmH_2O during quiet breathing but exceeds 10–15 cmH_2O during vigorous exercise [87] or hypercapnic stimulation [88]. Elite athletes can generate ΔPes higher than 50 cmH_2O during extreme exertion without sustaining lung injury [89]. However, in critically ill patients with inhomogeneous lung mechanics, ΔPes values below 3–5 cmH_2O and above 14–18 cmH_2O have been associated with excessively low and high effort, respectively [90–92]. Further, a Pmus between 5 and 10 cmH_2O and a PTP between 50 and 150 $cmH_2O{\cdot}sec{\cdot}min^{-1}$ could be considered within a desirable effort range [91, 92].

Esophageal manometry is a relatively non-invasive technique, particularly when integrated into a feeding tube. While its feasibility is greater in intubated patients, interpretation can be challenging, especially in the presence of expiratory muscle activity. With non-invasive respiratory support, additional challenges include calibration, patient discomfort, limited cooperation, and potential interface interference.

Alternative techniques for assessing inspiratory drive and effort

In the following sections, we discuss various alternatives to EAdi and esophageal manometry for estimating drive and effort. Sections are organized according to the neuroanatomical axis illustrated in Fig. 1. First, we will discuss methods that reflect the respiratory drive, which controls the respiratory muscle pump from upstream. Next, we will cover techniques that assess the work performed by the respiratory muscle pump and its immediate effects. Further, we will examine methods that look downstream from the respiratory muscle pump, focusing on variables influenced by inspiratory effort. For each technique, we outline the presumed (and sometimes debatable) reasons for using it, along with details on methods, data interpretation, and potential pitfalls. Clinical scoring systems that predict intubation, which might be due to excessive effort (respiratory rate-oxygenation [ROX] index, volume-oxygenation [VOX] index and heart rate, acidosis, consciousness, oxygenation, and respiratory rate [HACOR] score) and additional techniques, less commonly used in clinical practice, are presented in eFigure 2 and eTable 1 (Supplement).

Techniques for assessing inspiratory drive

Airway occlusion pressure (P0.1)

- Definition
  Reduction in Paw during the first 100 msec (0.1 s) of an occluded breath.
- Rationale
  With an occluded airway, changes in Paw equal ΔPes. A duration of 100 msec is too brief for the patient to perceive it consciously and thus does not influence the breathing pattern. With an occluded airway, there is no gas flow or change in lung volume. Therefore, P0.1 is not affected by vagal volume-related reflexes and respiratory system mechanics [93].
- Meaning
  Drive assessed by P0.1 was originally described as the initial mechanical component of the ventilatory response to hypercapnia [93]. With preserved neuromuscular coupling, it reflects the intensity of the motor output from the brainstem's respiratory centers [65, 93].
- Population
  Intubated patients.
- Measurement
  Apply a brief (< 250 msec) end-expiratory airway occlusion and measure the reduction in Paw during the first 100 msec of inspiration (Fig. 2). Some ventilators measure P0.1 with a proper occlusion started either manually or automatically. Others estimate it breath-by-breath during the trigger phase (often < 100 msec) and extrapolate it to 100 msec. This estimation can underestimate reference P0.1, particularly with high effort, flow triggering, or auto-PEEP [94, 95].
- Interpretation

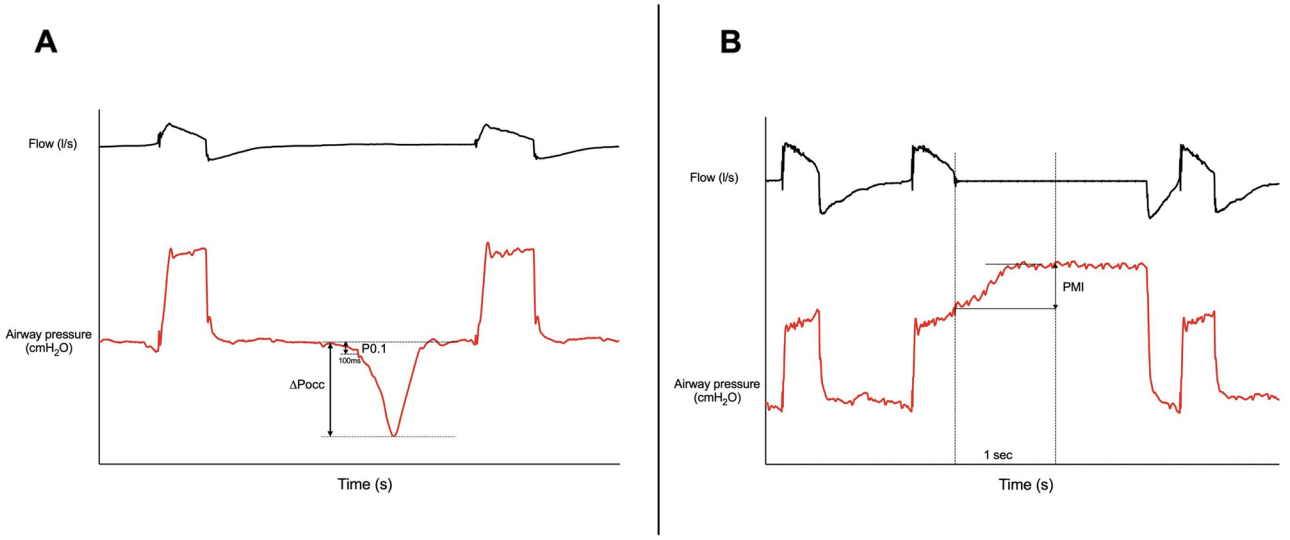

Fig. 2 Upper airway pressure trace **A.** How to measure P0.1 and whole-breath occlusion pressure (ΔPocc) during an end-expiratory occlusion. **B.** How to measure pressure-muscle-index (PMI) during an end-inspiratory occlusion. ΔPocc, whole-breath occlusion pressure; P0.1, airway occlusion pressure; PMI, pressure-muscle-index

Low and high drive can be suspected respectively when P0.1 is < 1.0 cmH_2O (corresponding to PTP/min < 50 cmH_2O*sec/min or change in transdiaphragmatic pressure [ΔPdi] < 3 cmH_2O) and > 3.5-4.0 cmH_2O (PTP/min ≥ 200–300 cmH_2O*sec/min or ΔPdi > 12 cmH_2O or work of breathing [WOB] < 0.75 J/L) [96–100]. A P0.1 > 3.5 cmH_2O has been associated with dyspnea and worse outcomes in invasively ventilated patients once able to communicate [99].

- Strengths and limitations
  P0.1 can be measured easily without specialized equipment. The accuracy of different ventilators and expiratory muscle activity need to be properly evaluated. Further, although partial neuromuscular blockade does not reduce P0.1—even at levels consistent with severe inspiratory muscle weakness [100]—it is possible that further deterioration, approaching complete paralysis, could eventually affect its accuracy. P0.1 is more useful as a screening tool for the extremes of effort, particularly low effort, rather than for precise estimation [94, 98]. A low P0.1 may indicate ventilatory over-assistance, excessive sedation, or severe muscle weakness. P 0.1 estimated without a 100msec occlusion (that is, during the trigger phase) should be interpreted with caution [101] especially with flow triggering or pressure triggering with high sensitivity (−1 or −2 cmH_2O) [94, 98]. Accuracy may be improved by switching ventilation to pressure triggering with low sensitivity (less than − 2 cmH_2O) for a few breaths [94, 98]. Ideally, this adjustment will prolong the duration of the trigger phase (closer to 100 msec) without significantly altering the breathing pattern of the patient.

Mean inspiratory flow (Vt/Ti)

- Definition
  Ratio of Vt to inspiratory time (Ti), expressed in liters per second.
- Rationale
  It represents the average flow rate of inspired air during the inspiratory phase of the breathing cycle, thereby expressing the speed of lung inflation.
- Meaning
  Vt/Ti reflects the balance between the neuromuscular drive and the mechanical properties of the respiratory system [44]. It is influenced by elastic and resistive loads, which modulate the inspiratory flow rate in response to mechanical constraints [102].
- Population
  Intubated and non-intubated patients during non-assisted breathing.
- Measurement
  Vt/Ti is measured using standard spirometry or ventilatory monitoring systems, obtained through breath-by-breath analysis. In mechanically ventilated patients, ventilators provide real-time Vt/Ti values [103].
- Interpretation
  Vt/Ti remains relatively stable within individuals, reflecting adaptations to metabolic demand and mechanical constraints [102]. In healthy subjects,

it ranges around 0.2–0.3 L/sec [104], while higher values (> 0.4 L/sec) have been associated with increased respiratory drive [105]. In COVID-19-related ARF, elevated Vt/Ti was observed in patients who required intubation [103].

- Strengths and limitations
  Vt/Ti is a non-invasive measure of inspiratory flow, easily derived from ventilator waveforms in non-assisted patients using pneumotachograph or spirometry. Unlike P.01, Vt/Ti is recorded during an entire inspiration with an open airway. It may underestimate the respiratory drive in patients without an intact inspiratory flow-generation pathway, such as those with severe muscle weakness or altered respiratory system mechanics [65].
  In this context, a normal or low Vt/Ti should be interpreted cautiously, while a high Vt/Ti will indicate an elevated (albeit underestimated) drive [106]. Interpretation is limited by neuromechanical coupling, lack of validated thresholds, and its inapplicability during assisted ventilation [105, 107].

Respiratory muscle surface electromyography (sEMG)

- Definition
  Transcutaneous measurement of the electrical activity of respiratory muscles [108].
- Rationale
  This electrical activity arises from action potentials triggering the contraction of respiratory muscles [108–111].
- Meaning
  Higher signal amplitude reflects greater muscle activation.
- Population
  Intubated and non-intubated patients.
- Measurement
  Common electrodes are carefully positioned over the respiratory muscles and connected to a dedicated monitor. Achieving optimal placement over the diaphragm is difficult.
- Interpretation
  Reference values are not available. Nevertheless, sEMG changes in line with EAdi and ΔPes within the same individual [111]. Signals can be calibrated against ΔPes during an end-expiratory occlusion, using the same method described for EAdi [111]. Values < 5 or > 10 cmH_2O of ΔPes estimated in this way may be considered too low or too high [74].
- Strengths and limitations
  Not widely available. Signal quality can be affected by various confounders [112]. Standardized methods and reporting have been proposed [108]. sEMG is reasonably accurate in tracking changes in respiratory muscle effort non-invasively and breath-by-breath [109, 111]. Accuracy can be improved by calibrating signal amplitudes to ΔPes. However, a key limitation is the inability to ensure that the recorded signal originates specifically from the diaphragm, as surface electrodes may also capture activity from adjacent muscles. This is relevant since other inspiratory muscles can contribute to generating Pmus [98, 111].

Techniques for assessing inspiratory effort

Whole-breath occlusion pressure (ΔPocc)

- Definition
  Maximum decrease in Paw during an entire occluded breath.
- Rationale
  With an occluded airway, changes in Paw accurately reflect ΔPes. A single random occlusion of the airway does not significantly alter the breathing pattern [113].
- Meaning
  ΔPocc adjusted for a correction factor reflects the effort during non-occluded breaths [113].
- Population
  Intubated patients.
- Measurement
  Apply an end-expiratory airway occlusion for one breath and measure the maximum decrease in Paw (Fig. 2). Estimate Pmus, ΔPes, and the $\Delta Plung_{dyn}$ during non-occluded breaths as follows:

$$Predicted\,\Delta Plung = \Delta Paw - Predicted\,\Delta Pes,$$
$$Predicted\Delta Plung = pressure\ support\ above\ PEEP - 2/3\Delta Pocc.$$

where ΔPocc is a negative number, reflecting a drop in Paw. The coefficients relating ΔPocc to the other variables were empirically derived and validated in two independent studies [98, 113].

- Interpretation
  ΔPocc more negative than − 15 or −20 cmH_2O predicts elevated diaphragmatic effort (ΔPdi > 12 cmH_2O) and total respiratory muscle effort (Pmus > 10–15 cmH_2O) [98, 113]. An estimated $\Delta Plung_{dyn}$ >20 cmH_2O reflects elevated $\Delta Plung_{dyn}$ as measured with esophageal manometry [98, 113]. ΔPocc less negative than − 7 cmH_2O indicates insufficient diaphragmatic activity (ΔPdi < 3 cmH_2O) [98].
- Strengths and limitations

ΔPocc can be measured easily without specialized equipment. P0.1 can be measured on the same Paw recording. ΔPocc is measured under quasi-static conditions, which—due to the force–velocity relationship—results in higher pressures than those generated by the same muscular effort during normal, quasi-isotonic breathing [71, 113]. The commonly used conversion coefficient (typically 3/4 that is < 1.0) accounts for this physiological difference and has shown remarkable consistency across studies [113]. However, the predicted Pmus reflects the effort performed during the few breaths immediately preceding the occluded breath—not the level of effort sustained over a longer period, which remains one of its main limitations. $\Delta Plung_{dyn}$ estimated from ΔPocc includes the pressure spent to overcome airway resistance during non-occluded breathing [114]. Higher resistive pressure is linked with more negative alveolar pressures [115] and increased pendelluft [116] potentially worsening stress and strain in the dependent lung [13, 116]. Finally, ΔPocc may underestimate effort in the presence of intrinsic PEEP not equilibrated at occlusion, as in dynamic hyperinflation.

Pressure-muscle-index (PMI)

- Definition
  Difference between the relaxed plateau airway pressure (Pplat) and the peak airway pressure generated by the ventilator.
- Rationale
  During an end-inspiratory airway occlusion, Paw stabilizes at the relaxed elastic recoil of the respiratory system (Pplat), which is the ratio of Vt to respiratory system compliance (Crs) plus PEEP. The difference between Pplat and the peak airway pressure generated by the ventilator reflects the gas volume actively inspired by the patient in addition to that delivered by the ventilator. Depending on Crs, this "extra" gas volume generates an "extra" elastic pressure known as the PMI [117, 118].
- Meaning
  PMI indicates the contribution of Pmus generated during inspiration (on top of the pressure delivered by the ventilator) to Pplat measured with the respiratory muscles fully relaxed, or the Vt actively inspired by the patient relative to the individual Crs.
- Population
  Intubated patients.
- Measurement
  Perform an end-inspiratory airway occlusion and measure the difference between Pplat and the peak airway pressure delivered by the ventilator (pressure support + PEEP) (Fig. 2). Expiratory cycling should be ≤ 25%. Measurements are reliable if: (i) time to reach Pplat < 800 msec; (ii) Pplat lasts > 2 sec; and (iii) Pplat varies < 0.6 cmH_2O/sec. [119]. From Pplat, static driving airway pressure (ΔPaw_{stat}) and Crs can be calculated using standard formulas [118, 120]. The Vt actively inspired by the patient is PMI*Crs.
- Interpretation
  A PMI < 0 cmH_2O (i.e., Pplat lower than peak airway pressure) indicates very low effort (PTP/min < 50 cmH_2O*sec/min and Pmus < 5 cmH_2O) [121] and ventilatory over-assistance [120, 122]. The threshold for strong efforts is poorly defined [117, 121]. Pplat and other derived variables can be interpreted as during controlled ventilation [118].
- Strengths and limitations
  PMI correlates with the elastic effort measured with esophageal manometry and surface electromyography [120, 121, 123–126] but neglects the (resistive) effort to overcome airway resistance. Excessively low values (< 0 cmH_2O) are better defined than excessively high values; therefore, PMI is particularly useful for detecting over-assistance [122]. The end-inspiratory occlusion method measures ΔPaw_{stat} and Crs during pressure-support ventilation [118, 120] which are clinically relevant [118]. Notably, these two parameters are computed assuming that total PEEP is the value set on the ventilator. This assumption becomes invalid when dynamic hyperinflation generates some auto-PEEP, which is difficult to measure during assisted ventilation. In this context, ΔPaw_{stat} will be overestimated, and Crs will be underestimated. Obtaining a reliable Pplat can be difficult [119] particularly when the effort is strong. Expiratory muscle contraction, which confounds the interpretation of PMI, can occur even with a stable Pplat [127]. A quality control algorithm can reduce the incidence of unreliable readings to < 10% [123, 128].

Nasal pressure swing (ΔPnose)

- Definition
  Maximum decrease in nasal pressure during tidal breathing.
- Rationale
  Alveolar pressure changes generated by spontaneous breathing are transmitted through the airway column to the nose.
- Meaning

ΔPnose reflects alveolar pressure changes generated by respiratory muscle effort.

- Population
  Non-intubated patients on HFNC or NIV.
- Measurement
  A nasal plug connected to a pressure transducer is inserted into one nostril to create a hermetic seal, while the other nostril remains open, and the mouth is kept closed. ΔPnose is measured as the maximum drop in pressure from end-expiratory values (Fig. 3, A).
- Interpretation
  In patients with hypoxemic ARF, ΔPnose correlates well with ΔPes (average ΔPes/ΔPnose ≈ 2.21) [128]. Values > 5.1 cmH_2O have been associated with HFNC failure [129] and increased need for respiratory support [130].
- Strengths and limitations
  The few publications on this technique originate from a single center, where ΔPnose was measured using a custom-made kit, primarily in COVID-19 patients. Accuracy can be affected by vigorous efforts, which may cause nasal valve collapse, airflow limitations, unfavorable nasal anatomy, or nasal congestion.

Diaphragm ultrasonography (USdi)

- Definition
  Diaphragm thickening fraction (TFdi) is the most studied parameter for estimating respiratory effort with ultrasound and is the focus of this section. Diaphragm excursion is inaccurate for effort assessment, especially during assisted ventilation when active displacement due to muscle contraction cannot be distinguished from passive displacement due to positive pressure ventilation. Diaphragm strain (speckle tracking) or shear modulus (shear wave elastography) are novel parameters for studying the mechanical properties of the diaphragm that warrants further validation [131].
- Rationale
  The diaphragm thickens when it contracts.
- Meaning
  Inspiratory diaphragm thickening reflects diaphragm contraction strength and respiratory muscle effort [132–134].
- Population
  Intubated and non-intubated patients.
- Measurement
  Diaphragm thickening fraction (TFdi) is typically measured using a linear probe in the right 10th intercostal space, along the mid-axillary line, and below the costophrenic sinus. The diaphragm is seen as a non-echogenic structure between the echogenic

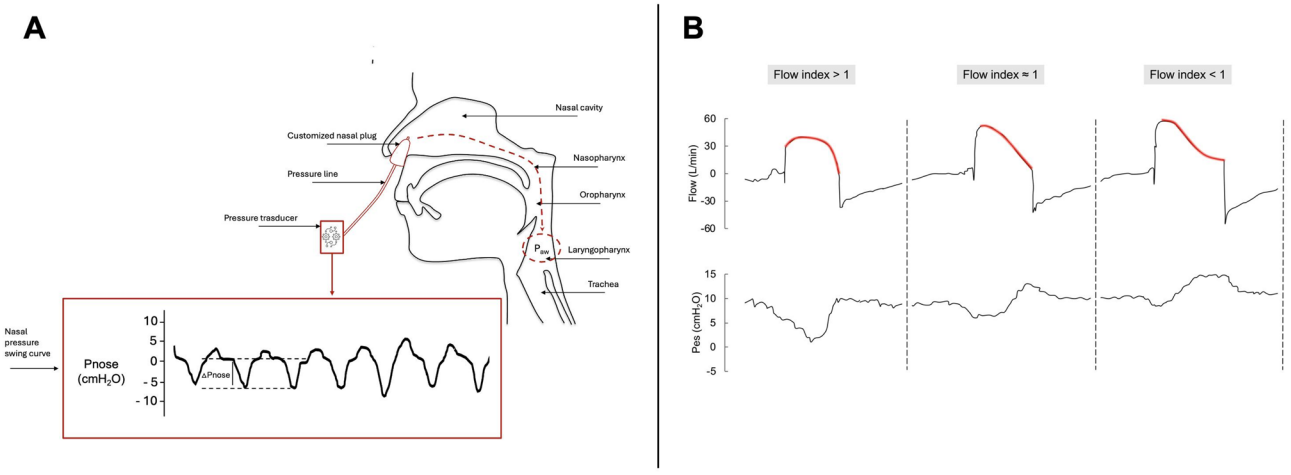

Fig. 3 **A**. Pnose assessment technique. This schematic illustrates the measurement of nasal pressure swing (ΔPnose) as a surrogate for inspiratory effort. The airway pressure (Paw) at the laryngopharyngeal level is influenced by inspiratory muscle activity and transmitted to the nasal cavity via the upper airway structures (nasopharynx, oropharynx, and laryngopharynx). A customized nasal plug is placed in the nostril and connected to a pressure line, which transmits pressure variations to a pressure transducer. The transducer records the nasal pressure swing curve, reflecting fluctuations in inspiratory effort over time **B.** Flow Index trace. Representative flow and esophageal pressure (Pes) tracings illustrating distinct inspiratory flow decay patterns, categorized by the Flow Index. The inpiratory flow decay phase is highlighted in red. The Flow Index is a unitless parameter that describes the shape of the inspiratory flow-time curve: a value > 1 (left panel) denotes a downward-facing concavity, indicative of sustained inspiratory effort delaying flow decay; a value ≈ 1 (middle panel) reflects an approximately linear decay, consistent with a minimally active patient; a value < 1 (right panel) corresponds to an upward-facing concavity, suggesting a passive patient. A higher Flow Index has been associated with higher inspiratory effort. ΔPnose, nasal pressure swing; Paw, airway pressure; Pes, esophageal pressure

peritoneum and diaphragmatic pleura [135]. TFdi is assessed as:

$$TFdi = [(end - inspiratory\,diaphragm\,thickness) - (end - expiratory\,diaphragm\,thickness)/(end - expiratory\,diaphragm\,thickness)] * 100$$

- Interpretation
  TFdi does not directly reflect diaphragmatic effort [136]. Instead, the relationship between TFdi over time and clinical outcomes in mechanically ventilated patients appears to follow a U-shaped pattern. Values < 15% or > 30–40% are associated with diaphragm thickness changes (either a decrease caused by atrophy or an increase due to load-induced injury) and prolonged mechanical ventilation. Intermediate values are associated with stable diaphragm thickness and the shortest duration of ventilation [31, 137].
- Strengths and limitations

This technique is safe and readily available. Data acquisition and analysis depend on the operator [10, 65] although good inter-assessor reliability can be achieved with short training and marking the probe placement site [132–134]. TFdi has not been consistently validated against absolute values of effort obtained through reference techniques [134, 138, 139]. For instance, in one study, the correlation between simultaneously measured TFdi and transdiaphragmatic pressure was only moderate in healthy subjects and weak in mechanically ventilated patients [136]. Several reasons may explain these findings. Imagining the zone of apposition in one dimension may be inadequate for studying the global function of the diaphragm in three dimensions. Factors such as lung hyperinflation, pleural effusions, abdominal hypertension, or obesity may affect the quality of the measurements. Passive thickening and diaphragm injury may confound the relationship between TFdi, active diaphragm contraction, and the resulting transdiaphragmatic pressure. While TFdi has been shown to correlate with EAdi in critically ill patients, this relationship is influenced by multiple factors, including diaphragm integrity, loading conditions, and patient effort variability [140]. TFdi does not consider extra-diaphragmatic muscle activity, which might also be assessed with ultrasonography [133]. Based on these limitations, TFdi might be more suitable for tracking changes within subjects (for instance, in response to changes in the level of support) than for quantitative comparisons between subjects.

Central venous pressure swing (ΔCVP)

- Definition
  Respiratory oscillation of CVP.
- Rationale
  Changes in pleural pressure are transmitted not only to the esophagus but also to the intrathoracic superior vena cava; they can be read as ΔCVP [91, 141–143]. During spontaneous inspiration, CVP decreases with effort.
- Meaning
  A larger ΔCVP reflects a larger pleural pressure drop due to a stronger effort [91, 141–143].
- Population
  Intubated and non-intubated patients with an intrathoracic central venous catheter.
- Measurement
  Maximum inspiratory fall, or negative deflection, of CVP from end-expiratory levels.
- Interpretation
  A ΔCVP > 10–15 cmH_2O suggests an elevated effort during unassisted breathing, CPAP, or pressure support ventilation (ΔPes > 10–15 cmH_2O) [91, 142, 144].
- Strengths and limitations
  A readily available method for patients who already have a central venous catheter in place. The relationship between ΔCVP and effort was strong in some studies but weak in others [117, 119] possibly due to variations in equipment, patient positioning, baseline CVP, intravascular volume, and cardiac function [141]. Not precise in predicting the exact strength of the effort.

BREF models

- Definition
  Two equations to predict the breathing effort during HFNC. They were developed using data from 260 patients studied with esophageal manometry and multivariable regression modelling. One equation estimates the actual ΔPes in cmH_2O, while the other estimates the risk of ΔPes being > 10 cmH_2O. Candidate predictors included age, sex, diagnosis of the novel coronavirus disease (COVID-19), heart rate, mean arterial pressure, respiratory rate, and the results of the arterial blood gas analysis. Final predictors were selected using a backward stepwise elimination strategy and include arterial base excess, respiratory rate and PaO_2/FiO_2 [145].
- Rationale
  ΔPes can be predicted by a combination of physiological variables readily available at the

bedside, which either depend on or reflect the respiratory effort [145].
- Meaning
  Respiratory muscle effort during HFNC.
- Population
  Non-intubated patients on HFNC.
- Measurement
  Both models are based on arterial base excess concentration, respiratory rate, and PaO_2:FiO_2. One of them also considers whether the patient has COVID-19. Other candidate predictors did not improve the accuracy of the estimates.
- Interpretation
  One (linear) model estimates the actual ΔPes in cmH_2O. The other (logistic) estimates the risk of ΔPes being > 10 cmH_2O (i.e., elevated) as a percentage (see eTable 2, supplement).
- Strengths and limitations
  The two equations require an arterial blood gas analysis. Their predictive performance is not optimal. An ongoing study (NCT06669312) will validate them and eventually incorporate additional predictors not available in the development dataset, such as the use of accessory muscles, the severity of dyspnea, and the severity of inflammation. It will also assess whether the BREF models outperform clinical judgment in predicting breathing effort.

Flow index

- Definition
  Unitless value indicating the shape of the descending portion of the inspiratory flow-time waveform. It equals 1 for a straight waveform, < 1 for upward-facing concavity, and > 1 for downward-facing concavity [146].
- Rationale
  During pressure support ventilation, when the patient is passive, the pressure gradient between the airway opening and the alveoli decays exponentially (upward-facing concavity) along with the inspiratory flow. In contrast, when the patient actively decreases alveolar pressure, this decay is delayed, and the shape of the inspiratory flow curve shifts to a downward-facing concavity.
- Meaning
  It measures the deviation of the descending portion of the inspiratory flow curve from the exponential decay (upward-facing concavity) typically observed in a passive patient. It indicates the patient's contribution in generating inspiratory flow alongside the ventilator.
- Population
  Intubated patients.
- Measurement
  It is calculated by fitting a non-linear model to the descending portion of the inspiratory flow-time waveform (Fig. 3, panel B).
- Interpretation
  Flow Index < 1 suggests a passive patient, while values > 1 are the result of inspiratory muscle activation, with higher values associated with higher effort [147]. Values < 2.1 or 2.6 could identify breaths with low inspiratory effort (Pmus < 5 cmH_2O) [147, 148]. Values < 4.5 can rule out the presence of high inspiratory effort (Pmus > 10 cmH_2O) [147]. Values within the range between these two thresholds (i.e., from 2.1-2.6 to 4.4) could be considered ideal.
- Strengths and limitations
  The Flow Index algorithm is not yet available on ventilators; however, its visual inspection can still provide qualitative insights into inspiratory effort, although this needs validation. It is particularly useful for screening low inspiratory effort and ruling out high effort. The Flow Index reflects solely the inspiratory effort made after the activation of the inspiratory trigger, when the inspiratory flow begins. Therefore, it may be more appropriate for evaluating the adequacy of the inspiratory support level.

Techniques for assessing inspiratory drive and effort based on their consequences.

Tidal volume

- Definition
  The volume of gas that enters and exits the lungs during each respiratory cycle.
- Rationale
  Gas inflation depends on the pressure gradient created by the ventilator (which raises the pressure at the airway opening) and/or the respiratory muscles (which lowers the alveolar pressure). An effort that significantly reduces alveolar pressure will result in a larger Vt.
- Meaning
  During assisted spontaneous breathing, a large Vt may signal a strong effort, particularly when accompanied by altered respiratory mechanics (i.e., low compliance/high resistance as is often the case during hypoxemic ARF) and low ventilator assistance. However, high Vt may also result from excessive ventilator support with minimal muscular effort. In clinical practice, observing changes in Vt and respiratory effort in response to a brief reduction in pressure support may help distinguish between

active (patient-driven) and passive (ventilator-driven) high Vt patterns [120].
- Population
  Primarily, patients connected to a ventilator, possibly including those on NIV.
- Measurement
  Modern ventilators display the Vt breath-by-breath as the integral of gas flow over time. Calibrating the ventilator, minimizing air leaks, and considering expired rather than inspired Vt are key factors.
- Interpretation
  In patients with ARF receiving NIV, a Vt > 9.0-9.5 ml/kg of predicted body weight despite low support can be associated with a higher risk of intubation and death, particularly among those with moderate-to-severe hypoxia, possibly because of increased effort [11, 149, 150].
- Strengths and limitations
  Monitoring Vt is straightforward in intubated patients, manageable during NIV (if leaks are minimal), and challenging in other conditions [151–155]. The relationship between Vt, respiratory effort, and outcome is complex. Vt depends on the interplay between the respiratory drive, ventilator assistance, respiratory muscle effort, and respiratory system mechanics (Fig. 4). Its relationship with the effort is not linear. An elevated Vt does not necessarily indicate high respiratory effort, particularly when ventilatory assistance effectively unloads the respiratory muscles. For example, NIV may still prevent intubation despite high Vt if muscle unloading is achieved (so that respiratory effort is actually low) [9, 156, 157].

Electrical impedance tomography (EIT)

- Definition
  Transcutaneous measurement of relative changes of thoracic electrical impedance.
- Rationale
  Air transmits electrical signals poorly. Changes in impedance across the thorax parallel changes in gas volume inside the lungs.
- Meaning
  EIT monitors the regional distribution of ventilation and changes in end-expiratory lung volume [158]. For the same ventilator assistance and respiratory system mechanics, global changes in impedance (and Vt) reflect global changes in effort. EIT also allows recognition of high regional Vt, airflows, and occult pendelluft, which may signal excessive local effort.
- Population
  Intubated and non-intubated patients.
- Measurement
  The technique requires an electrode belt around the patient's chest and a dedicated monitor. Regional changes in impedance are visualized as numbers and images. Absolute Vt can be obtained after calibration, even in non-intubated patients [154]. However, its accuracy is only temporarily stable, as changes in respiratory mechanics can alter the calibration conversion factor [158].
- Interpretation
  EIT may unveil the benefits and harms of spontaneous breathing in patients with ARF. For example, decreasing the ventilator assistance may result in a more homogenous ventilation distribution and better oxygenation [159]. On the other hand, a stronger effort in the dorsal lung can lead to gas influx from the ventral lung (occult pendelluft), regional overdistention, and impaired carbon dioxide clearance [13, 160, 161].
- Strengths and limitations
  EIT is a radiation-free technique that provides continuous insight into regional phenomena at the bedside. It requires specialized equipment. It does not measure the effort itself but how that effort affects alveolar recruitment and ventilation distribution. Occult pendelluft may signal a strong effort. Monitoring lung volumes with EIT can be especially important for non-intubated patients, as their airway pressure and expired gas volumes cannot be directly measured. However, its application in spontaneously breathing patients presents challenges in ensuring reliable data acquisition, as not all EIT-derived parameters are validated for this context [158].

Dyspnea

- Definition
  Breathing discomfort or "the symptom that conveys an upsetting or distressing experience of breathing awareness" [26].
- Rationale
  Dyspnea might be linked to the sensation of "too much effort to breathe".
- Meaning
  Dyspnea may signal excessive respiratory muscle effort.
- Population
  Intubated and non-intubated patients. Ideally, the patient should be able to communicate.
- Measurement
  If the patient can communicate, assess for dyspnea by asking a dichotomous question such as "Is your

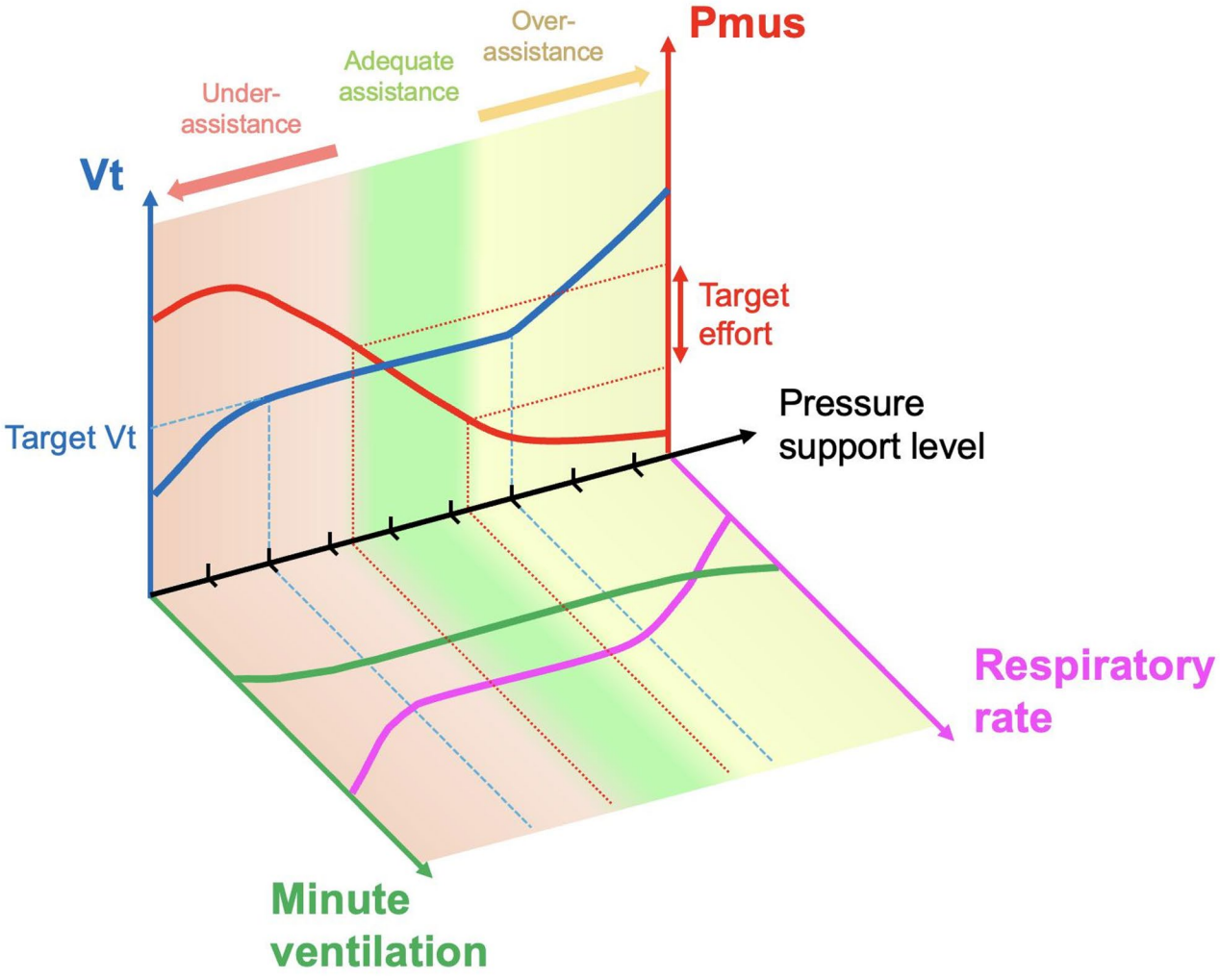

Fig. 4 Schematic representation of patient-ventilator interactions during pressure support ventilation. Within a certain range of assistance, Vt matches the level set by the respiratory drive. Adjusting pressure support results in an opposite change in the inspiratory effort, with minimal changes in Vt. This specific range includes "adequate assistance", where the effort to reach the target Vt is tolerable. This condition varies among individuals and is influenced by factors such as respiratory drive, the impedance of the respiratory system, and the muscle capacity of the patient. When pressure support exceeds this range, the inspiratory effort decreases significantly, resulting in "over-assistance". If pressure support continues to increase, Vt will passively rise. Conversely, with "under-assistance", the inspiratory effort to achieve the target Vt significantly increases. In extreme cases, the respiratory muscles may become unable to sustain the excessive load, causing Vt to ultimately fall short of the target. Please note that some patients may have a respiratory drive and target Vt that are too high to be achieved with a tolerable effort; even with high pressure support, under-assistance may occur. Vt, tidal volume. Pmus, respiratory muscle pressure (a measure of respiratory effort).
Adapted from Docci et al. [122]

breathing comfortable?". If dyspnea is present, evaluate its intensity using a 100-mm visual analogue scale or a 0–10 numerical rating scale [162, 163]. If the patient cannot communicate, use an observation scale such as the Intensive Care-Respiratory Distress Observation Scale (IC-RDOS) [164, 165] and the Mechanical Ventilation-Respiratory Distress Observation Scale (MV-RDOS) [166].

- Interpretation
  Dyspnea increases with the respiratory drive [99, 167, 168]. As long as a high drive results in increased effort, dyspnea signals an increased effort (see eTable 3, Supplement for details).
- Strengths and limitations
  Dyspnea primarily indicates a mismatch between respiratory drive (target ventilation) and actual ventilation [26, 65, 169, 170]. It is more associated with "not getting enough air" than with "too much effort to breathe", and it does not correlate with more objective measures of effort [170, 171]. Dyspnea may arise when the patient generates insufficient effort for the drive, regardless of the effort. Moreover, psychological factors such as anxiety

or distress may act as confounders, amplifying the perception of dyspnea independently of physiological determinants.

How to integrate assessment of inspiratory drive and effort in clinical practice

Various techniques have been developed to measure patient's breathing effort along the respiratory drive cascade. Selecting one or another relies on several factors: patient's characteristics (e.g., intubated vs. non-intubated), clinical setting (e.g., ICU vs. non-ICU) and team expertise (e.g., respiratory intensivists vs. general physicians), therapeutic goals (e.g., care escalation vs. de-escalation), and often resource availability (e.g., high- vs. middle- or low-income settings). To frame the choice at the bedside, key practical considerations should include the following: which patients is it suitable for? Are there thresholds to rely on? Does stronger or weaker evidence support the technique? Notably, the techniques described in this review differ markedly in validation status, clinical uptake, and strength of supporting evidence. Among the most extensively studied are P0.1, ΔPocc, PMI, USdi and, to a lesser extent, ΔCVP. These methods have been evaluated in multiple physiological and clinical investigations and are routinely used in research and bedside settings. By contrast, other techniques—such as ΔPnose, the flow index, and the BREF models—are still in early phases of clinical development. Their use has been reported in a small number of studies, often limited to specific populations (e.g., patients with COVID-19); while promising, their performance remains to be systematically validated. A summary table (Table 1) presents the current features of each technique based on these criteria that could help physicians choose one over the others.

At the bedside of critically ill intubated patients, assessment of respiratory effort aims at optimizing ventilatory strategies, tailoring support and guiding de-escalation. The esophageal pressure–time product could be seen as the most accurate measure of work of breathing. However, its reliance on complex calculations limits its use to research purposes rather than routine bedside practice. This may change with the emergence of ventilators equipped with integrated esophageal pressure monitoring algorithms. When available in experienced hands, ΔPes should be the first choice as a surrogate means of

Table 1 Techniques for assessing inspiratory drive and effort at the bedside: clinical applicability, validation, and available thresholds

Technique	Target population	Need for specialized equipment other than a ventilator	Validation (relative to other methods)	Threshold for low effort/overassistance	Threshold for high effort/underassistance
Reference methods					
Pes	Intubated/non-intubated	Yes	Very high	< 3–5 cmH_2O [90, 92]	>14–18 cmH_2O [90, 92]
EAdi	Intubated/non-intubated	Yes	Very high	EAdi-derived ΔPes < 5 cmH_2O [74]	EAdi-derived ΔPes > 10 cm H_2O [74]
Assessing respiratory drive					
P0.1	Intubated	No	High	< 1.0 cmH_2O [94, 96, 98]	> 3.5-4.0 cmH_2O [94, 96]
Vt/Ti	Intubated/non-intubated	No	Moderate	Undefined	Undefined
sEMG	Intubated/non-intubated	Yes	Moderate	sEMG-derived ΔPes < 5 cmH_2O [74, 98, 111]	sEMG-derived ΔPes > 10 cmH_2O [74, 98, 111]
Assessing muscle effort					
ΔPocc	Intubated	No	High	Less negative than − 7 cmH_2O [90, 104]	More negative than − 15 to −20 cmH_2O [90, 104]
PMI	Intubated	No	Moderate	< 0 cmH_2O [120, 122]	Undefined
ΔPnose	Non-intubated (HFNC)	Yes	Low	NA	> 5.1 cmH_2O [128]
BREF models	Non-intubated (HFNC)	No	Low	NA	Estimated ΔPes > 10 cmH_2O [145]
USdi	Intubated/non-intubated	Yes	Moderate	TFdi < 15%	TFdi > 30-40%
ΔCVP	Intubated/non-intubated	No	Moderate	Undefined	> 10–15 cmH_2O [132]
Flow index	Intubated	No*	Low	< 2.1–2.6 cmH_2O [147, 148]	>4.5 cmH_2O [147, 148]
Assessing the consequence of effort					
Vt	Intubated/non-intubated (NIV)	No	Low	Undefined	> 9.0-9.5 ml/kg of predicted body weight
EIT	Intubated/non-intubated	Yes	Low	Undefined	Undefined
Dyspnea	Intubated/non-intubated	No	Low	Undefined	Dyspnea-VAS > 3 and NRS ≥ 4 are associated with high P0.1 [159, 160]

*Visual inspection of waveform shape does not require specialized equipment, while numerical quantification relies on a dedicated algorithm

PTP. In parallel, EAdi represents the most direct bedside measure of central respiratory drive. In the absence of EAdi, P0.1 may offer a practical surrogate for assessing respiratory drive, although it should be interpreted cautiously and, when possible, integrated with additional assessments of respiratory muscle activity. These include PMI, which estimates elastic workload during assisted breaths, and ΔPocc, a surrogate for elastic and resistive load, when esophageal manometry is not available. Though widely accessible, direct Vt assessment could serve primarily as an indicator rather than a precise measure of effort.

In non-ICU settings, where resources are limited and patients are non-intubated, early recognition of high-risk patients is critical yet challenging. Only a few techniques are available, and they are not very accurate at assessing drive and effort. Dyspnea evaluation and the BREF models may serve as first-line screening tools, followed by targeted instrumental assessments addressing at least one dimension of respiratory effort—airway pressure, muscle activity, or volume. USdi offers a rapid and practical approach to assessing muscle function (especially in patients without pressure support), while Pnose could provide a rough estimate of effort. Volume-based assessments, although feasible, lack a direct correlation with effort.

General principles for assessing inspiratory drive and effort at the bedside

While the choice of method depends on factors such as accessibility, patient tolerance, ease of interpretation, and clinical applicability, the assessment of respiratory drive and effort should be guided by a set of overarching principles. These principles apply regardless of the chosen technique and are essential for ensuring a meaningful evaluation at the bedside. A schematic overview is provided in Fig. 5.

1. *Define the clinical question*. If precise quantification is required, esophageal manometry remains the gold standard for studying and accurately assessing inspiratory effort. However, alternative techniques may offer more practical solutions for identifying extreme effort levels and guiding clinical decisions regarding the escalation or de-escalation of respiratory support [172].
2. *Begin with clinical assessment and trust the gestalt it provides* [173, 174]. Signs like labored breathing, diaphoresis, and accessory muscle use provide critical insights that instrumental data should confirm or, when contradictory, prompt reassessment [175]. This approach seems particularly relevant in non-intubated patients, where objective monitoring is limited.
3. *Use ventilator waveforms as an extension of physical examination*. Although not a quantitative measure of effort, ventilator waveforms offer real-time, continuous insight into patient–ventilator interaction and the presence of either excessive or insufficient support. A structured waveform-based method has been validated against esophageal pressure, with excellent performance in identifying the timing of respiratory effort and detecting both major and minor asynchronies [176]. Careful observation of pressure-, flow-, and volume-time curves can indeed reveal important clues about the underlying inspiratory drive and muscular effort. For instance, signs of over-assistance may include a prolonged insufflation time and late cycling during pressure support ventilation [35], passive flow profiles, and absent or minimal negative deflection on the pressure-time curve. Conversely, features such as high inspiratory flow rates, early cycling, and—during square-flow assisted ventilation—a scooped appearance of the pressure waveform [177] may suggest under-assistance or strong spontaneous drive. These waveform patterns, when interpreted alongside the clinical context can integrate more direct assessments of drive and effort and may help guide timely ventilator adjustments even in the absence of advanced monitoring tools.
4. *Avoid reliance on a single technique*, as each method has specific limitations and biases [18, 22].
5. *Consider evolution over time*. Allow a stable breathing pattern to emerge, average at least 3–5 breaths, and use repeated measurements to capture dynamic changes.
6. *Mind the gap between research and real life*. To date, most studies on respiratory effort have focused on intubated patients, excluding those with COPD and fibrosis, in which lung mechanics differ significantly.

Knowledge gaps and avenues for research

The role of high inspiratory effort in lung and diaphragm injury remains unclear, with P-SILI supported mainly by indirect evidence [10, 178]. Moreover, the dissociation between drive and effort complicates patient assessment [179] particularly in non-intubated individuals, underscoring the need for monitoring both parameters. Whether respiratory drive and effort primarily reflect disease severity or actively contribute to lung injury remains unresolved, as their causal role is difficult to isolate in clinical or experimental settings. Finally, caution is needed when targeting respiratory drive and effort. If they cause lung injury, controlling them within physiological limits may improve outcomes. However, if they merely reflect the severity of the underlying disease, suppressing them without addressing their cause could

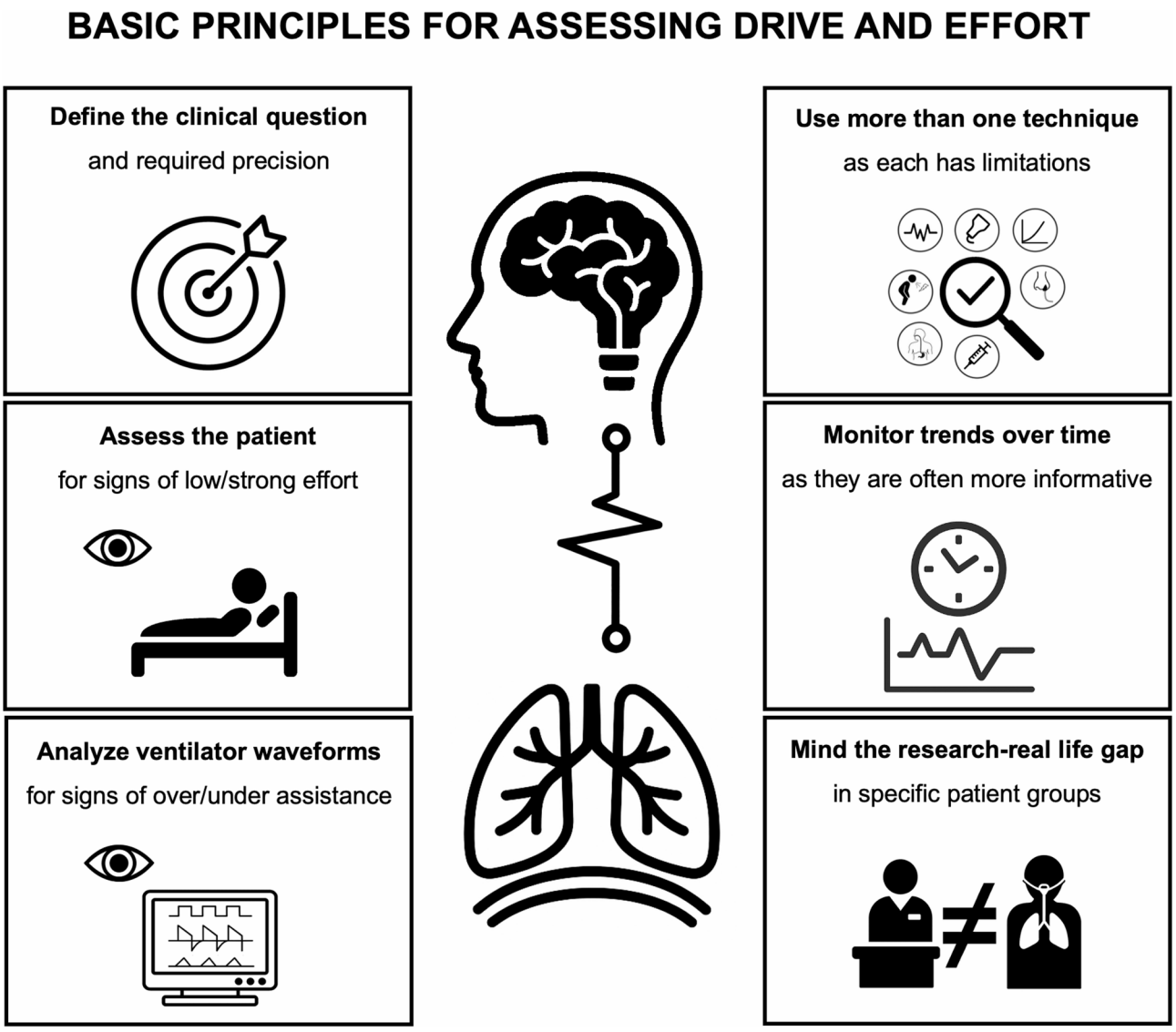

Fig. 5 Key points for bedside assessment of inspiratory drive and effort. This schematic highlights essential principles to guide clinical evaluation of inspiratory drive and effort at the bedside. These include: (1) defining the clinical question and the level of precision required; (2) assessing the patient for clinical signs of low or strong effort; (3) analyzing ventilator waveforms for clues of under- or over-assistance; (4) integrating multiple monitoring techniques, as each has limitations; (5) considering trends over time, which are often more informative than isolated measurements; and (6) recognizing the gap between research data and real-life patients, particularly in underrepresented populations such as those with COPD or fibrotic lung disease. COPD, chronic obstructive pulmonary disease

worsen the prognosis. Additionally, there is no consensus on the optimal bedside technique for assessing inspiratory effort, which limits clinical decision-making. While interventions targeting low drive (e.g., reduced sedation, early assisted ventilation) or excessive effort (e.g., personalized PEEP, awake prone positioning) have been proposed, physiological gaps must be addressed to prevent misapplication of potentially beneficial treatments. Future research should focus on (1) establishing consensus-based recommendations on the most appropriate techniques for measuring drive and effort according to setting and scope; (2) standardizing assessment methods to improve study reproducibility and facilitate clinical integration. Researchers in the field should be actively engaged in achieving these goals. A structured dissemination and refinement of inspiratory drive and effort assessment beyond research applications should be encouraged, as bedside integration may aid in improving the management of patients with ARF.

Abbreviations

ARDS	acute respiratory distress syndrome
ARF	acute respiratory failure
AUROC	area under the receiver operating characteristics
COPD	chronic obstructive pulmonary disease

Crs	compliance of the respiratory system
ΔCVP	central venous pressure swing
EAdi	electrical activity of the diaphragm
ECG	electrocardiogram
Ecw	chest wall elastance
EIT	electrical impedance tomography
FRC	functional residual capacity
Flow(t)	inspiratory flow
HACOR	heart rate, acidosis, consciousness, oxygenation, respiratory rate
HFNC	high-flow nasal cannula
ICU	intensive care unit
MV	mechanical ventilation
NAVA	neurally adjusted ventilatory assist
NME	neuromechanical efficiency
NIV	non-invasive mechanical ventilation
NRS	numeric rating scale
Paw	airway pressure
ΔPaw	airway pressure swing
Pcw	chest wall recoil pressure
ΔPes	esophageal pressure swing
Pdi	transdiaphragmatic pressure
ΔPdi	transdiaphragmatic pressure swing
PEEP	positive end-expiratory pressure
Pga	gastric pressure
$Plung_{dyn}$	dynamic transpulmonary pressure
$\Delta Plung_{dyn}$	dynamic transpulmonary driving pressure
PO_2	partial pressure of oxygen
PMI	pressure-muscle-index
Pmus	respiratory muscle pressure
P0.1	airway occlusion pressure
ΔPocc	whole-breath occlusion pressure
Pplat	plateau airway pressure
Ppl_{FRC}	passive pleural pressure at FRC
P-SILI	patient self-inflicted lung injury
PTP	pressure-time product
Rcw	resistance of the chest wall
ROI	region of interest
ROX	respiratory rate-oxygenation
RR	respiratory rate
sEMG	surface electromyography
TFdi	diaphragm thickening fraction
US	ultrasound
USdi	diaphragm ultrasonography
VOX	volume-oxygenation
Vt	tidal volume
Vte	expiratory tidal volume
WOB	work of breathing

Supplementary Information

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Supplementary Material 1

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Author contributions
RT, AP, and TM conceptualized the review, authored the ***Background and rationale***, ***How to integrate assessment of inspiratory drive and effort in clinical practice***, ***General principles for assessing inspiratory drive and effort at the bedside***, and ***Knowledge gaps and avenues for research***paragraphs, sections on Vt/Ti and Flow index, eTable 2, Figure 3, panel A, Figure 5 and critically revised and edited the final manuscript. ES and LH authored the ***Pathophysiology*** paragraph and critically revised and edited the final manuscript. AJ authored the ***Clinical Relevance*** and ***Reference method for assessing the inspiratory drive: diaphragm electrical activity*** t paragraphs and critically revised and edited the final manuscript. LB authored the ***Clinical relevance*** paragraph and critically revised and edited the final manuscript. DLG, EA, and TY authored the ***Reference method for assessing theinspiratory effort: esophageal manometry*** paragraph, produced eFigure 1 and critically revised and edited the final manuscript. IT, ZJ-X, EG, EC, and MD were responsible for the sections on P0.1, PMI, ΔPocc, and ΔPnose, produced Figure 2 and 3, and critically revised the manuscript. LPiq, SM, JB, GG and AR authored the sections on EMG, EAdi, USdi, and ΔCVP and critically revised the manuscript. GC, LL, and GB authored the sections on Vt, EIT, and VOX, produced Figure 4, and critically revised and edited the final manuscript. OR, AD, and LPis wrote the sections on ROX, HACOR, BREF, and Dyspnea, produced eTable 1 and 3 critically revised and edited the final manuscript. JP produced Figure 1, Figure 3, panel B, eFigure 2, critically reviewed the manuscript and edited the final version. For the equal contribution in conceptualization and drafting of the manuscript, RT and AP share first authorship. All authors have read and approved the final version.

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Data availability
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Declarations

Ethics approval and consent to participate
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Consent for publication
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Competing interests
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