REVIEW

Expiratory muscle dysfunction in critically ill patients: towards improved understanding

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Abstract

Introduction: This narrative review summarizes current knowledge on the physiology and pathophysiology of expiratory muscle function in ICU patients, as shared by academic professionals from multidisciplinary, multinational backgrounds, who include clinicians, clinical physiologists and basic physiologists.

Results: The expiratory muscles, which include the abdominal wall muscles and some of the rib cage muscles, are an important component of the respiratory muscle pump and are recruited in the presence of high respiratory load or low inspiratory muscle capacity. Recruitment of the expiratory muscles may have beneficial effects, including reduction in end-expiratory lung volume, reduction in transpulmonary pressure and increased inspiratory muscle capacity. However, severe weakness of the expiratory muscles may develop in ICU patients and is associated with worse outcomes, including difficult ventilator weaning and impaired airway clearance. Several techniques are available to assess expiratory muscle function in the critically ill patient, including gastric pressure and ultrasound.

Conclusion: The expiratory muscles are the "neglected component" of the respiratory muscle pump. Expiratory muscles are frequently recruited in critically ill ventilated patients, but a fundamental understanding of expiratory muscle function is still lacking in these patients.

Keywords: Expiratory muscles, Acute respiratory failure, Mechanical ventilation, Respiratory muscle weakness, Respiratory muscle monitoring

Introduction

The respiratory muscle pump drives alveolar ventilation and is therefore of vital importance. The diaphragm, rib cage muscles and abdominal wall muscles are the most important components of the respiratory muscle pump [1]. Recruitment of each muscle depends on the (relative) load imposed on the respiratory system, lung volume, and the phase of the respiratory cycle. An acute imbalance between respiratory muscle load and capacity will result in respiratory failure and, ultimately, the need for mechanical ventilation. Many studies and reviews have focused on diaphragm structure and function in patients with acute respiratory failure, including critically ill patients [2–11]. However, the role of expiratory muscles in the physiology of breathing in acute respiratory failure is largely neglected in the literature. This is surprising, given the important role of these muscles in respiration, especially in patients with impending respiratory failure.

The aim of the current paper is to discuss the role of the expiratory muscles in respiration, in particular in critically ill patients in whom respiratory muscle weakness develops rapidly, and may thus have a large clinical impact. We will also describe techniques used to evaluate expiratory muscle function in intensive care unit (ICU) patients. We will not focus in detail on the role of

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the expiratory muscles in coughing or maintaining body position.

Physiology of expiratory muscle recruitment

The expiratory muscles include those of the abdominal wall (transversus abdominis muscle, internal oblique muscle, external oblique muscle, and rectus abdominis muscle) and some of the rib cage ones (e.g., the internal intercostal muscles and the triangularis sterni muscle) [1, 12–16] (Fig. 1). During tidal breathing, the expiratory muscles are largely inactive, although the transversus abdominis muscle may occasionally show some activity during quiet breathing [16]. Also, in the upright position, the abdominal wall muscles exhibit tonic activity to counteract the gravitational forces acting on the abdominal contents and thus to maintain the diaphragm at optimal length for pressure generation [17–19].

Figure 2 shows the physiology of expiratory muscle recruitment. Activation of the expiratory muscles during breathing occurs when the (relative) load imposed on the inspiratory muscles increases. High absolute respiratory loading may occur under different conditions, such as exercise, low respiratory system compliance, and intrinsic positive end-expiratory pressure (PEEPi). Low inspiratory muscle capacity (high relative load on inspiratory muscles) is common in ICU patients due to ICU-acquired respiratory muscle weakness [20]. In the presence of an imbalance between inspiratory muscle load and capacity, the abdominal wall muscles are

Take home message

The expiratory muscles are the "neglected component" of the respiratory muscle pump. This narrative review summarizes the physiology and pathophysiology of expiratory muscles in critically ill ventilated patients. Techniques to monitor expiratory muscle function in these patients are also discussed.

recruited during expiration in a fixed hierarchy [21–24]: initially the transversus abdominis muscle, followed by the internal oblique muscle and the external oblique muscle, and finally the rectus abdominis muscle [16, 17, 25]. Activation of the abdominal wall muscles increases abdominal pressure in the expiratory phase. As the diaphragm is relaxed during (most of the) expiratory phase, this increased abdominal pressure is transmitted to the pleural space, consequently reducing the expiratory transpulmonary pressure, which helps to deflate the lung (less pulmonary hyperinflation/lung strain). Furthermore, increased abdominal pressure enhances inspiratory muscle capacity via at least two mechanisms. First, increased abdominal pressure moves the diaphragm at end expiration to a more cranial position, which results in a more optimal length for tension generation [26, 27]; second, when the end-expiratory lung volume falls below functional residual capacity (FRC), elastic energy is stored in the respiratory system. This stored energy facilitates the next inspiration (i.e., allows more rapid and greater development of negative pleural pressure) [28,
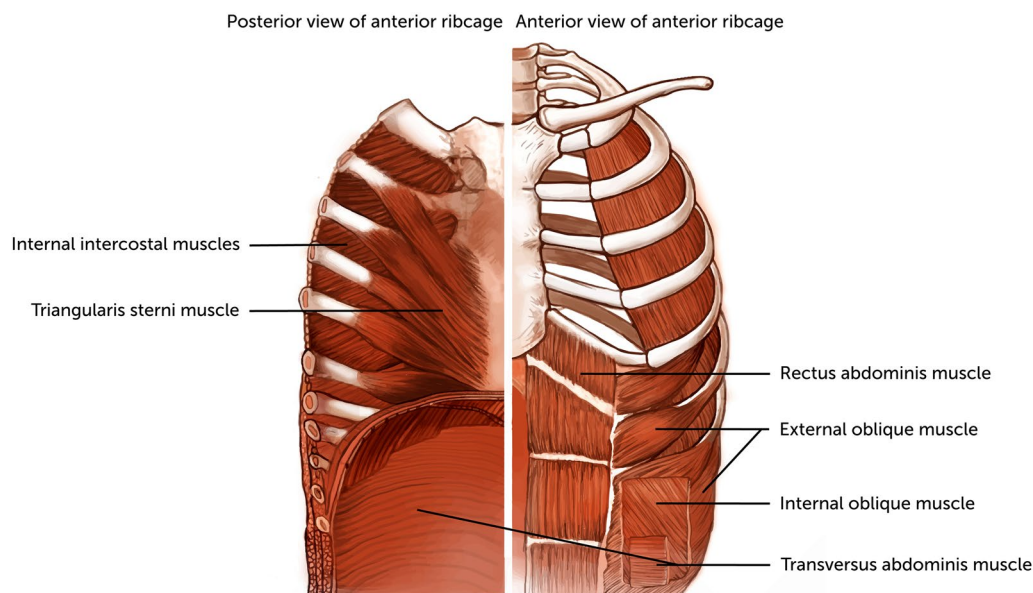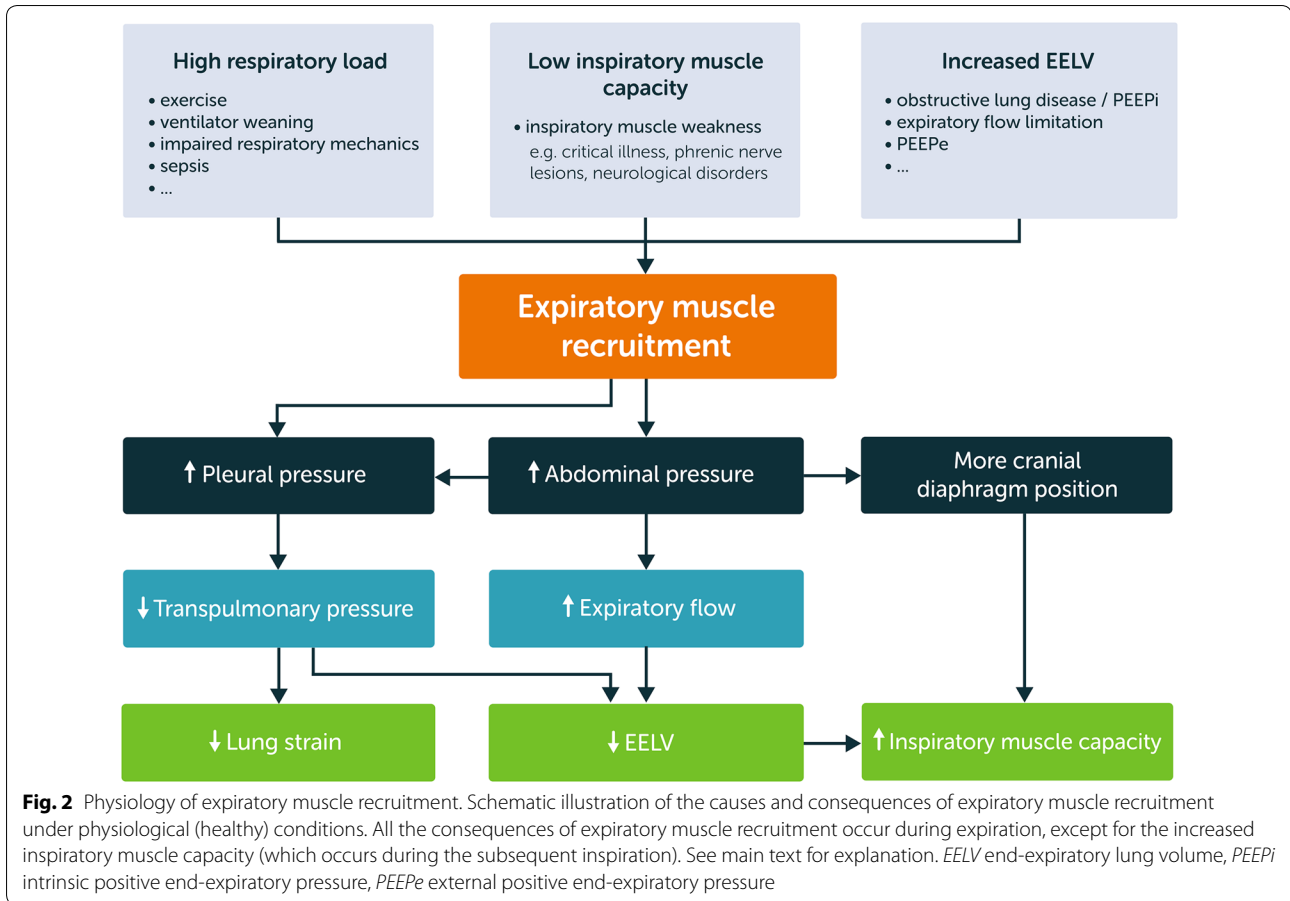

Fig. 1 The expiratory muscles of the respiratory muscle pump. The respiratory muscle pump is a complex organ that involves a large number of muscles that contribute to inspiration or expiration. This figure schematically demonstrates the expiratory muscles. With the exception of the diaphragm, other inspiratory muscles are not shown

Fig. 2 Physiology of expiratory muscle recruitment. Schematic illustration of the causes and consequences of expiratory muscle recruitment under physiological (healthy) conditions. All the consequences of expiratory muscle recruitment occur during expiration, except for the increased inspiratory muscle capacity (which occurs during the subsequent inspiration). See main text for explanation. *EELV* end-expiratory lung volume, *PEEPi* intrinsic positive end-expiratory pressure, *PEEPe* external positive end-expiratory pressure

29]. In fact, during strenuous inspiratory loading up to 28% of tidal volume is generated below FRC, which can be attributed to expiratory muscle contraction [21].

It should be recognized that isolated contraction of the abdominal expiratory muscles causing an increase in abdominal pressure and pleural pressure would result in chest wall distortion, in particular expansion of the lower rib cage. This would likely increase the elastic inspiratory work of breathing and flatten the diaphragm. To limit distortion of the lower rib cage during active expiration, the internal intercostal muscles are recruited to stabilize the rib cage [1].

In addition to an imbalance between inspiratory muscle load and capacity, an increased end-expiratory lung volume, as in application of positive end-expiratory pressure (PEEP), may also recruit the abdominal wall muscles (Figs. 2 and 3) [30]. For example, in patients with normal respiratory system compliance (i.e., 80 mL/cmH$_2$O), application of 10 cmH$_2$O of PEEP would, theoretically, increase end-expiratory lung volume by 800 mL (in the absence of airway closure). However, a physiological feedback mechanism invo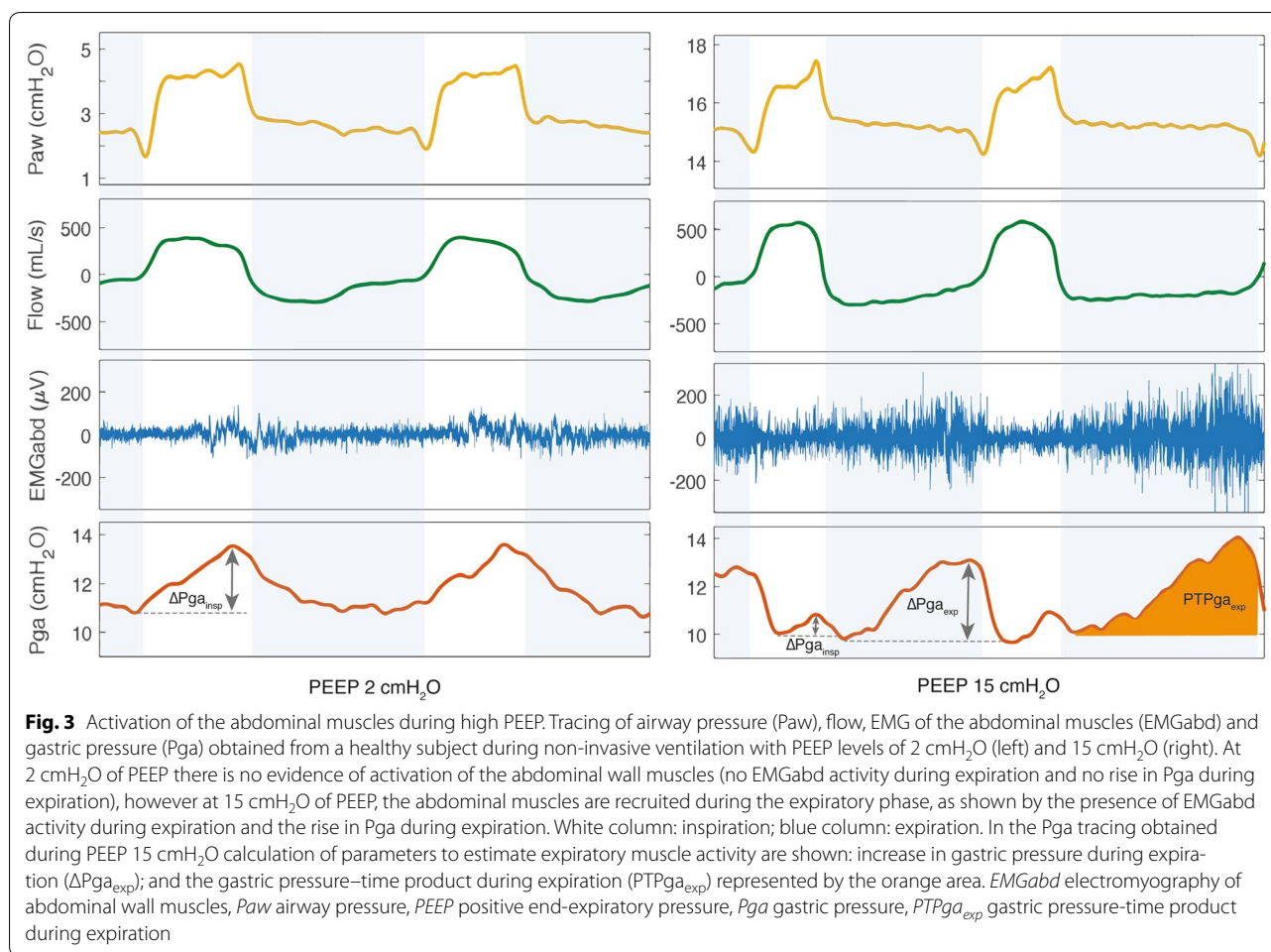lving vagal pathways or proprioceptive influences limits the increase in end-expiratory lung volume by activation of the abdominal wall muscles during expiration, and thus protects against high lung strain [31, 32].

Another fundamental role of the expiratory muscles is to develop effective cough pressure to facilitate airway clearance [33]. Contraction of the expiratory muscles against a closed airway may increase the intrathoracic pressure may increase to as high as 300 mmHg within 0.2 s. Once the glottis is open, a very high expiratory flow (up to 720 L/min) can be generated [33, 34]. Expiratory muscle weakness reduces cough strength and peak flow velocity, predisposing patients to pneumonia and atelectasis [33, 35, 36].

Undesirable effects of expiratory muscle recruitment

Recruitment of the expiratory muscles during expiration may have undesirable effects in critically ill patients (Fig. 4 and Table 1).

First, in patients with acute respiratory distress syndrome (ARDS) or atelectasis, increased pleural pressure during expiration resulting from expiratory muscle recruitment may result in negative transpulmonary

Fig. 3 Activation of the abdominal muscles during high PEEP. Tracing of airway pressure (Paw), flow, EMG of the abdominal muscles (EMGabd) and gastric pressure (Pga) obtained from a healthy subject during non-invasive ventilation with PEEP levels of 2 cmH$_2$O (left) and 15 cmH$_2$O (right). At 2 cmH$_2$O of PEEP there is no evidence of activation of the abdominal wall muscles (no EMGabd activity during expiration and no rise in Pga during expiration), however at 15 cmH$_2$O of PEEP, the abdominal muscles are recruited during the expiratory phase, as shown by the presence of EMGabd activity during expiration and the rise in Pga during expiration. White column: inspiration; blue column: expiration. In the Pga tracing obtained during PEEP 15 cmH$_2$O calculation of parameters to estimate expiratory muscle activity are shown: increase in gastric pressure during expiration (ΔPga_{exp}); and the gastric pressure–time product during expiration ($PTPga_{exp}$) represented by the orange area. *EMGabd* electromyography of abdominal wall muscles, *Paw* airway pressure, *PEEP* positive end-expiratory pressure, *Pga* gastric pressure, *PTPga$_{exp}$* gastric pressure-time product during expiration

pressure during expiration, leading to cyclic alveolar collapse or airway closure and thereby facilitating small airway and alveolar injury [37–40]. Consistent with this reasoning, a recent study in ARDS patients demonstrated a higher expiratory transpulmonary pressure in patients receiving neuromuscular blockers compared with control patients (1.4 ± 2.7 cmH$_2$O versus -1.8 ± 3.5 cmH$_2$O, respectively, $p = 0.02$) [41]. Interestingly, neuromuscular blockers also abolish expiratory activity of the diaphragm (if present) [42] which is expected to decrease expiratory transpulmonary pressure. However, the pressure generated by the diaphragm in the expiratory phase is relatively low compared with that generated by the expiratory muscles. Therefore, the effects of neuromuscular blockers on expiratory transpulmonary pressure largely depend on the relaxation of the expiratory muscles.

Second, expiratory flow limitation is a condition in which expiratory flow cannot be increased, despite an increase in expiratory driving pressure (pressure difference between alveoli and mouth during expiration) [43]. Typically, this occurs in patients with emphysema,

but it may also occur during tidal breathing in patients with expiratory muscle activity. The exact mechanism is unclear, but it has been proposed that dynamic airway compression plays an important role [44] (Fig. 5). Elevated pleural pressure during active expiration decreases the airway transluminal pressure, which subsequently may compress the collapsible part of the airway. Total airway collapse is prevented as increased pleural pressure is also transmitted to the alveoli/airways (for an extensive discussion see also [43]). Expiratory airway compression may result in elevated end-expiratory lung volume and PEEPi [43], especially in patients with chronic obstructive pulmonary diseases (COPD) and in patients failing ventilator weaning [24, 45].

Third, in patients weaning from mechanical ventilation, expiratory muscle recruitment is expected when an imbalance exists between the respiratory load and inspiratory muscle capacity. Indeed, activation of the expiratory muscles has been demonstrated during ventilator weaning, especially in patients failing a weaning trial [22–24]. We recently found that expiratory muscle
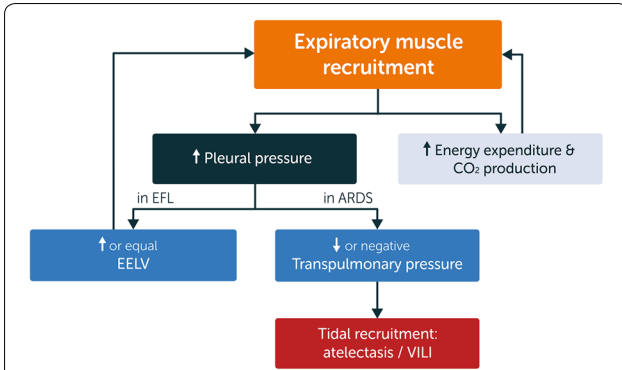
Fig. 4 Pathophysiology of expiratory muscle recruitment. Schematic illustration of the pathophysiological consequences of expiratory muscle recruitment in critically ill patients. The depicted relationships are mostly hypothetical due to the low number of studies on expiratory muscle function in ICU patients. The elevated pleural pressure caused by expiratory muscle recruitment might lead to dynamic airway collapse, especially in patients who already have expiratory flow limitation (EFL). This leads to an equal or increased end-expiratory lung volume (EELV). On the other hand, elevated pleural pressure might lead to negative expiratory transpulmonary pressures, especially in diseases with an increased lung elastance such as in ARDS, which in turn leads to atelectasis and tidal recruitment. *EFL* expiratory flow limitation, *ARDS* acute respiratory distress syndrome, *VILI* ventilator-induced lung injury

Table 1 Clinical impact of expiratory muscle dysfunction

Clinical event	Expiratory muscles-related mechanisms
Weaning failure/extubation failure	Increased respiratory energy consumption, ineffective cough, inability to improve diaphragm efficiency
Atelectasis/pneumonia	Ineffective cough
Small airway and alveolar injury	Negative expiratory transpulmonary pressure resulting in alveolar collapse and/or airway closure
Pulmonary hyperinflation	Inability to increase expiratory flow

effort progressively increased throughout the trial in such patients [24]. The neuromuscular efficiency of the diaphragm was lower in weaning failure patients compared with weaning success patients, which challenges the concept that expiratory muscle activation improves diaphragm contractile efficiency [24], although this requires further evaluation. Nevertheless, recruitment of the expiratory muscles during a weaning trial appears to be a strong marker of weaning failure.

Technically, expiratory muscle activity interferes with the assessment of PEEPi.

PEEPi can be measured using different techniques. In patients with expiratory muscle activity, an end-expiratory occlusion will be highly influenced and exaggerated by the contraction of the expiratory muscles [46]. Similarly, the relaxation of the expiratory muscles at the beginning of the effort explains part of the initial drop in esophageal pressure, which is not entirely explained by so-called dynamic PEEPi. Either the drop in gastric pressure (Pga) or the rise in Pga during expiration must be subtracted from the esophageal drop in order to measure a reliable PEEPi [47].

Expiratory muscle strength in critically ill patients

Several studies have demonstrated the development of expiratory muscle weakness in critically ill patients [48–62, 64]. Most studies used the maximum expiratory pressure (MEP) as a marker of expiratory muscle strength [48–57]. Despite the heterogeneity of the studies in terms of populations and measurement techniques, the MEP was lower than the reference values [63] in all studies that obtained MEP at the time of ventilator weaning [48–55, 64]. Patients failing extubation exhibit a lower MEP (mean decrease varying from 9 to 31 cmH$_2$O) compared with extubation success patients [48–55, 64]. This indicates that expiratory muscle weakness is a potential predictor of weaning outcome. How expiratory muscle weakness affects weaning and extubation outcome is largely unknown. Potential explanations include inadequate secretion clearance and insufficient cough capacity resulting in atelectasis, reduced contractile efficiency of the diaphragm, or inadequate reduction of PEEPi.
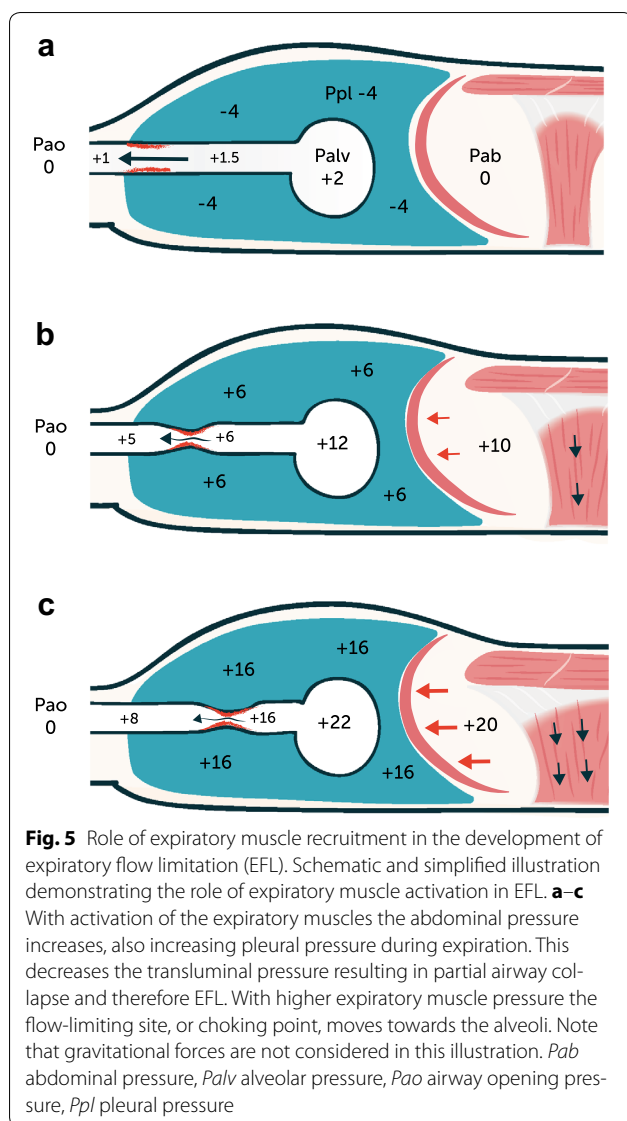
Remarkably, no studies have investigated the association between diaphragm weakness and expiratory muscle weakness.

Risk factors for expiratory muscle weakness in critically ill patients

Risk factors for the development of ICU-acquired weakness of the peripheral muscles and diaphragm have been discussed recently [2, 4, 57, 65]. Whether these risk factors also have an impact on the expiratory muscles is largely unknown. We briefly discuss risk factors that may contribute to the development of expiratory muscle weakness.

Sepsis

Sepsis and systematic inflammation have been linked to the development of muscle weakness, including weakness of the expiratory muscles [2, 61, 65]. Sepsis induces a severe and persistent increase in protein catabolism, resulting in muscle wasting and muscle weakness [59, 60]. Compared with non-septic surgical patients, the

Fig. 5 Role of expiratory muscle recruitment in the development of expiratory flow limitation (EFL). Schematic and simplified illustration demonstrating the role of expiratory muscle activation in EFL. **a**–**c** With activation of the expiratory muscles the abdominal pressure increases, also increasing pleural pressure during expiration. This decreases the transluminal pressure resulting in partial airway collapse and therefore EFL. With higher expiratory muscle pressure the flow-limiting site, or choking point, moves towards the alveoli. Note that gravitational forces are not considered in this illustration. *Pab* abdominal pressure, *Palv* alveolar pressure, *Pao* airway opening pressure, *Ppl* pleural pressure

rectus abdominis muscle from surgical patients with sepsis showed significantly lower in vitro contractility [59]. In addition, the reduced MEP (≤ 30 cmH$_2$O) found at the time patients regained normal consciousness showed an independent association with septic shock [57].

Mechanical ventilation

Mechanical ventilation plays an important role in the development of diaphragmatic dysfunction in critically ill patients [2, 9, 10, 66]. Potential mechanisms include disuse atrophy due to ventilator over-assist, or load-induced injury as a result of ventilator under-assist. The impact of mechanical ventilation on expiratory muscles has not been systematically investigated. However, as mentioned earlier, ventilator settings including PEEP

and the level of inspiratory assist may have an impact on the activity of the expiratory muscles (Fig. 3) [46, 67], although the ultimate impact of mechanical ventilation on expiratory muscle strength is largely unknown and should be further investigated.

Other risk factors

Co-morbidities, such as COPD and myopathies, or complications such as intra-abdominal hypertension, may put patients at increased risk of ICU-associated expiratory muscle weakness [68, 69]. Drugs such as sedatives, neuromuscular blockers and corticosteroids have been shown to affect peripheral muscle function and diaphragm muscle function in ICU patients [2, 65, 70]. The effects of these drugs on expiratory muscle function have not been systematically studied.

Strategies to maintain or improve expiratory muscle strength

Strategies that aim to improve diaphragm function [71, 72] may also benefit the expiratory muscles, although clinical studies are lacking. The feasibility of neuromuscular electrical stimulation to reduce expiratory muscle atrophy in ICU patients is under investigation (NCT 03453944).

Quantification of expiratory muscle effort in critically ill patients

While visual inspection of the trunk and palpation of the abdominal wall may reveal activation of the expiratory muscles, they do not allow quantification of effort. In this section, we summarize the main clinical techniques that can be used to quantify expiratory muscle effort in ICU patients.

Gastric pressure

Activation of the abdominal wall muscles increases abdominal pressure. Changes in Pga during expiration reflect changes in abdominal pressure and can thus be used to quantify expiratory muscle effort [22, 24, 39, 63, 73]. Pga is measured using an air-filled balloon catheter inserted into the stomach. Bladder pressure has also been proposed as a means of quantifying intra-abdominal pressure [74, 75], and showed an acceptable correlation with Pga in supine position (bias $= 0.5$ mmHg, and precision $= 3.7$ mmHg (limits of agreement, -6.8 to 7.5 mmHg)) [74]. To quantify the effort of expiratory muscles, Pga amplitude and the Pga pressure–time product (PTP) during expiration can be calculated (Fig. 3).

Amplitude of gastric pressure

Both the rise in Pga over the course of expiration [46] and the drop in Pga at the onset of the next inspiration [76] have been used to quantify the activity of the expiratory muscles. However, only the expiratory increase in Pga showed a good correlation with the electromyographic amplitude of the transverse abdominis muscle (correlation coefficient ranging from 0.70 to 0.95) [77].

Pressure–time product

The PTP of the expiratory muscles has been quantified using the area enclosed by the esophageal pressure curve and the static chest-wall recoil pressure curve during expiration [78]. The PTP accounts for the energy expenditure during both the isometric and dynamic phases of expiration (independently of volume displacement). However, expiratory esophageal pressure only represents the pressure generated by the abdominal wall muscles when the diaphragm is completely relaxed [39, 79]. As diaphragm activity has been demonstrated during expiration [42, 67], abdominal wall muscle effort cannot be reliably quantified using the expiratory esophageal PTP alone. Therefore, it is recommended to use the expiratory Pga in order to calculate the PTP of the expiratory muscles [80–83]. The gastric PTP can be obtained from the area under the expiratory Pga curve, in which the baseline is defined as the resting end-expiratory Pga from the preceding breath [24, 80, 81].

Work of breathing

Traditionally, the Campbell diagram is used to quantify the inspiratory work of breathing [84], but it allows estimation of the expiratory work as well. The area of the esophageal pressure–volume loop at the right side of the chest wall relaxation curve represents expiratory muscle effort [85, 86]. By definition, work is performed only when there is volume displacement (work = pressure × volume). However, as explained above, during dynamic airway collapse part of the pressure generated by the expiratory muscles does not result in lung volume displacement, and therefore the Campbell diagram underestimates the total effort of the expiratory muscles [44, 87]. Under these circumstances, the PTP may better reflect expiratory muscle effort.

Volitional tests of expiratory muscle strength

The MEP is the most widely used measure of expiratory muscle strength [63]. Standard procedures for non-intubated subjects have been established [63]. For intubated patients, the MEP can be measured using a unidirectional valve that allows inspiration but prevents expiration [48, 51, 88]. Some investigators coached subjects to perform an expiratory effort against an occluded airway for 25 to 30 s, and then recorded the most positive pressure developed [48, 51, 88]. Calculating the ratio of maximum inspiratory pressure to MEP is a simple way to assess the relative impairment of the inspiratory muscles versus the expiratory muscles [89]. As MEP measurement requires a voluntary patient effort, this might not be feasible in a proportion of ICU patients. As an alternative to MEP, cough pressure can be assessed to quantify expiratory muscle strength [33, 63, 73].

Cough test

The cough test is a relatively easy-to-perform, complementary test for the diagnosis of expiratory muscle weakness. Both cough pressure measured via air-filled balloons in the stomach or esophagus, and cough peak expiratory flow measured at the opening of an endotracheal tube or using the ventilator flow sensor [90], are feasible in ICU patients. In patients unable to cooperate, a cough may be induced either by instilling physiological saline [35] or by advancing a suctioning catheter through the patient's tube [36].

Abdominal wall muscle ultrasound

Ultrasound has become a popular tool for quantifying changes in the thickness and activity of the diaphragm in ICU patients [3, 91, 92], but few studies have used this technique to evaluate the expiratory muscles. Abdominal ultrasound allows direct visualization of the three layers of the abdominal wall muscles and the rectus abdominis muscle [93–96] (Fig. 6). In our experience, the abdominal wall muscles are easy to visualize using ultrasound, and measurement of thickness is feasible in almost all patients. In healthy subjects, the thickness of individual abdominal wall muscles follows a certain pattern: transversus abdominis < external oblique < internal oblique < rectus abdominis [96]. The thickness of the transversus abdominis muscle measured with ultrasound is strongly correlated with the pressure developed during an expiratory maneuver (assessed by the change in Pga) [94]. In addition, the transversus abdominis muscle thickness increase is significantly correlated with the muscle's electrical activity [93]. However, all these studies were performed in healthy subjects, and further studies are needed to determine the reliability and validity of ultrasound assessment of expiratory muscle thickness and function in ICU patients.

Other diagnostic tests

Electrical and magnetic stimulation of the abdominal wall muscles are other methods used to quantify the strength of these muscles [25, 79, 81]. As these techniques are
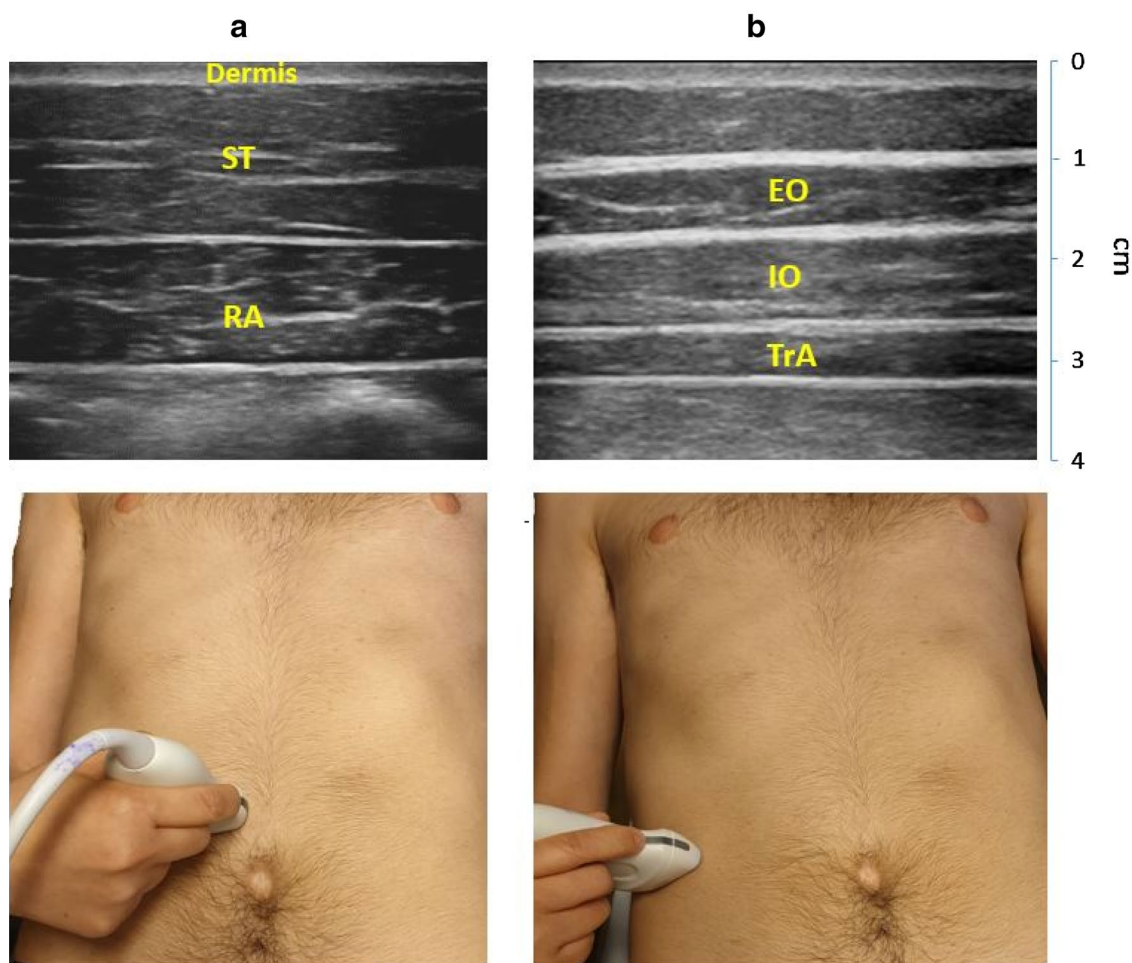
Fig. 6 Ultrasound image of the abdominal muscles. Left: ultrasound image of the rectus abdominis muscle (RA) (top), obtained with the probe placed 2–3 cm above the umbilicus and 2–3 cm from the midline (bottom). Right: ultrasound image of the external oblique muscle (EO), internal oblique muscle (IO) and transversus abdominis muscle (TrA) (top), obtained with the probe placed midway between the costal margin and the iliac crest, along the anterior axillary line (bottom)

cumbersome and uncomfortable, they are rarely used either in clinical practice or for research purposes.

Electromyography of the expiratory muscles has been used in research settings to study the timing of expiratory muscle recruitment during respiration [17, 77], but has not reached clinical implementation. Therefore, these techniques are beyond the scope of this review.

Conclusions

The expiratory muscles are the "neglected component" of the respiratory muscle pump. Rather as the heart does not comprise only a left ventricle, but also a right one, the respiratory muscle pump is much more than just the diaphragm. In this paper, we have summarized the physiology and pathophysiology of expiratory muscles, with a special focus on critically ill patients. Expiratory

muscles are frequently recruited in critically ill ventilated patients, but a fundamental understanding of expiratory muscle function is still lacking in these patients. Gastric pressure monitoring provides multiple bedside parameters for analysis of expiratory muscle effort, but their clinical implications need to be established.

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