



Monitoring and preventing diaphragm injury

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Purpose of review

The present review summarizes developments in the field of respiratory muscle monitoring, in particular in critically ill patients.

Recent findings

Patients admitted to the ICU may develop severe respiratory muscle dysfunction in a very short time span. Among other factors, disuse and sepsis have been associated with respiratory muscle dysfunction in these patients. Because weakness is associated with adverse outcome, including prolonged mechanical ventilation and mortality, it is surprising that respiratory muscle dysfunction largely develops without being noticed by the clinician. Respiratory muscle monitoring is not standard of care in most ICUs. Improvements in technology have opened windows for monitoring the respiratory muscles in critically ill patients. Diaphragm electromyography and esophageal pressure measurement are feasible techniques for respiratory muscle monitoring, although the effect on outcome remains to be investigated.

Summary

Respiratory muscle dysfunction develops rapidly in selected critically ill patients and is associated with adverse outcome. Recent technological advances allow real-time monitoring of respiratory muscle activity in these patients. Although this field is in its infancy, from a physiological perspective, it is reasonable to assume that monitoring respiratory muscle activity improves outcome in these patients.

Keywords

electromyography, esophageal pressure, mechanical ventilation, monitoring, respiratory muscles

INTRODUCTION

Monitoring can be arbitrarily defined as a (nearly) continuous evaluation of the physiological functions of a patient in real time to guide management decisions, including therapeutic interventions, and assessment of those interventions [1]. In practice, it is not easy to distinguish between monitoring and diagnostic testing, and, in fact, they may overlap. Monitoring vital functions is the hallmark of modern intensive care. In the majority of ICU patients, vital functions are monitored using invasive and noninvasive equipment. In very few ICUs, however, respiratory muscle activity is routinely monitored. Reasons for not monitoring may include unawareness of the effects of critical illness on the respiratory muscles, underestimating the importance of respiratory muscle dysfunction on patient outcome, lack of evidence that monitoring improves outcome and technical difficulties [2]. It is our opinion that monitoring respiratory muscle activity should be considered in a selected group of ventilated ICU patients.

EFFECTS OF CRITICAL ILLNESS ON THE RESPIRATORY MUSCLES

Acute ventilatory failure is among the most common reasons for ICU admission. In these patients, the respiratory muscle pump cannot meet the demands because of excessive loading, weakness or, less common, reduced central drive. Unloading of the respiratory muscles by mechanical ventilation is lifesaving in these patients. Recent studies, however, have demonstrated that both critical illness and mechanical ventilation may have adverse effects on the respiratory muscles. In-depth discussion of the pathophysiological mechanisms is beyond the scope of the present article [3[•]]. Briefly, in a landmark paper, Levine *et al.* [4] reported the

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KEY POINTS

- Respiratory muscle weakness frequently develops in critically ill patients and is associated with adverse outcome.
- Development of respiratory muscle weakness in these patients goes largely unnoticed because monitoring tools are infrequently used to assess respiratory muscle activity.
- Diaphragm electromyography and esophageal pressure measurement are feasible tools to monitor respiratory muscle activity in ventilated patients.
- Despite the strong rationale for monitoring, no studies have been conducted to evaluate the effect of respiratory muscle monitoring on outcome in critically ill patients.

development of muscle fiber atrophy and activation of proteolytic enzymes in the human diaphragm after only 18–69 h of controlled mechanical ventilation. Subsequent studies [5] showed that 5–6 days of controlled mechanical ventilation reduce pressure-generating capacity of the diaphragm by $\pm 30\%$. Moreover, Demoule *et al.* [6¹¹] found that force-generating capacity of the diaphragm is already impaired at ICU admission, in particular in patients with sepsis, suggesting the development of septic respiratory muscle myopathy. This is important because several studies have shown that respiratory muscle weakness is associated with adverse outcome, including longer duration of mechanical ventilation and mortality [5,7,8].

It is therefore remarkable that ICU-acquired respiratory muscle weakness largely develops out of the clinician's sight. No monitoring tool is used to assess respiratory muscle activity. In contrast, a patient with acute circulatory failure would likely be monitored with an intra-arterial catheter, continuous electrocardiogram and possibly a pulmonary artery catheter to evaluate the response to therapeutic interventions, despite the absence of evidence that these devices improve outcome in large groups of patients. It is, however, likely that additional physiological data are helpful to the clinician if interpreted appropriately.

TECHNIQUES FOR RESPIRATORY MUSCLE MONITORING

Today, various tools are available to evaluate respiratory muscle activity and function. These techniques have been used extensively for research purposes but have not really found their way into

clinical routine. In general, the ideal monitoring device allows tracking of respiratory muscle activity or function during the period a patient is admitted to the ICU. Additional features should include minimal invasiveness, easy and real-time interpretation of the data and no interference with routine clinical care or mobilization. Table 1 summarizes techniques to assess respiratory muscle function and activity. Below, we will discuss only those techniques that are feasible in clinical care.

Pressure and flow

Monitoring pressure and flow in the thoracic cage or ventilator circuit is widely used to assess respiratory muscle activity.

Ventilator waveforms

Modern ventilators continuously display pressure and flow as measured within the ventilator circuit. The pressure reported by the ventilator is the final result of a complex interaction between the patient and the ventilator. Observing ventilator pressure tracing would be an attractive monitoring technique because it is available in every patient, real time, noninvasive and at low cost. Ventilator waveform analysis, however, is not a very sensitive method for the assessment of respiratory muscle activity. In an elegant study, Colombo *et al.* [9] demonstrated that even experienced intensivists have difficulty recognizing activity of the respiratory muscles during mechanical ventilation from the airway pressure and flow signals of the ventilator. For experienced intensivists, the sensitivity for detecting asynchrony between respiratory muscle activity and ventilator support was approximately 28%, obviously much too low for a reliable monitoring tool.

Esophageal and transdiaphragmatic pressure

Esophageal pressure (Pes) provides an estimate of pleural pressure [10¹²] and has been used for decades in physiological studies and more recently in clinical studies in ICU patients [11]. When both Pes and gastric pressure (Pga) are measured simultaneously, transdiaphragmatic pressure (Pdi) can be calculated ($Pes - Pga$), which is a specific measure of diaphragm activity. Pes and Pga can be measured by using air-filled or liquid-filled balloons attached to a nasogastric tube connected to a pressure transducer. Nasogastric feeding tubes with esophageal and gastric balloons are commercially available, and some ventilators (i.e. Hamilton G5) have auxiliary ports for the continuous measurement of Pes. Otherwise,

Table 1. Techniques to assess respiratory muscle function and activity

Technique	Comment	Monitoring	Diagnostic testing
Airway pressure and flow waveforms	Real time available in most ventilators, but of limited value in monitoring respiratory muscle function (see main text)	+	+
Occlusion pressure ($P_{0.1}$)	Used as an index for neural respiratory drive. Real time available in most mechanical ventilators, but not specific for respiratory muscle function	-	+
Esophageal (and gastric) pressure waveforms	Available in real time. Useful for detecting and quantifying respiratory muscle function (discussed in detail in main text). A (double) balloon catheter is required	+++	+++
Maximal (sniff) inspiratory/expiratory maneuvers	These maneuvers are useful for quantifying global respiratory muscle function. High values exclude respiratory muscle weakness, whereas low values may reflect poor technique or effort instead of respiratory muscle weakness. Cumbersome to perform in critically ill patients	-	+
Magnetic twitch airway pressure/transdiaphragmatic pressure	Nonvoluntary specific evaluation of diaphragm function using magnetic phrenic nerve stimulation, fairly invasive and technically difficult. Magnetic twitch airway pressure is without balloon catheter	-	++
Diaphragm EMG (EAdi)	Specific measure of neural respiratory drive (discussed in detail in main text). Real time available on only one ventilator, requires esophageal catheter with electrodes	+++	++
Ultrasonography (B/M-mode)	Well characterized, noninvasive and easy to perform at the bedside, but real time not available (see main text)	+	+++
Chest X-ray and fluoroscopy	Used for detection of diaphragm paralysis. Atelectasis and diaphragmatic eventration may complicate findings. Misleading in patients with bilateral paralysis. High radiation exposure with fluoroscopy	-	+/-

EAdi, electrical activity of the diaphragm; EMG, electromyography.

stand-alone pressure transducers are needed. Clinical trials [12] have demonstrated that prolonged P_{es} measurement is feasible in ICU patients. Practical issues related to the choice of catheter type, positioning and validation have recently been described [10¹¹].

Solid-state transducers for P_{es} measurement are used in gastroenterology, but because of fragility and high costs, these transducers are less suitable for monitoring purposes in the ICU. Because most ventilated patients need a nasogastric tube for feeding anyway, a dedicated feeding tube with balloons does not pose an additional patient risk.

Monitoring P_{es} can be used to track and even quantify activity of the inspiratory and expiratory

muscles and detect patient-ventilator asynchrony (Fig. 1).

More in-depth analysis of P_{es} over time may provide valuable information including the work of breathing and energy expenditure [13]. Today, no software is available to calculate these sophisticated parameters in real time. In addition, interpretation of the data is rather complex and therefore not yet suitable for routine monitoring. When P_{es} is used to monitor respiratory muscle activity, a simple algorithm should be adopted, as discussed below. In addition, but beyond the scope of the present article, P_{es} can be used to calculate transpulmonary pressure, intrinsic positive end-expiratory pressure and respiratory mechanics [14].

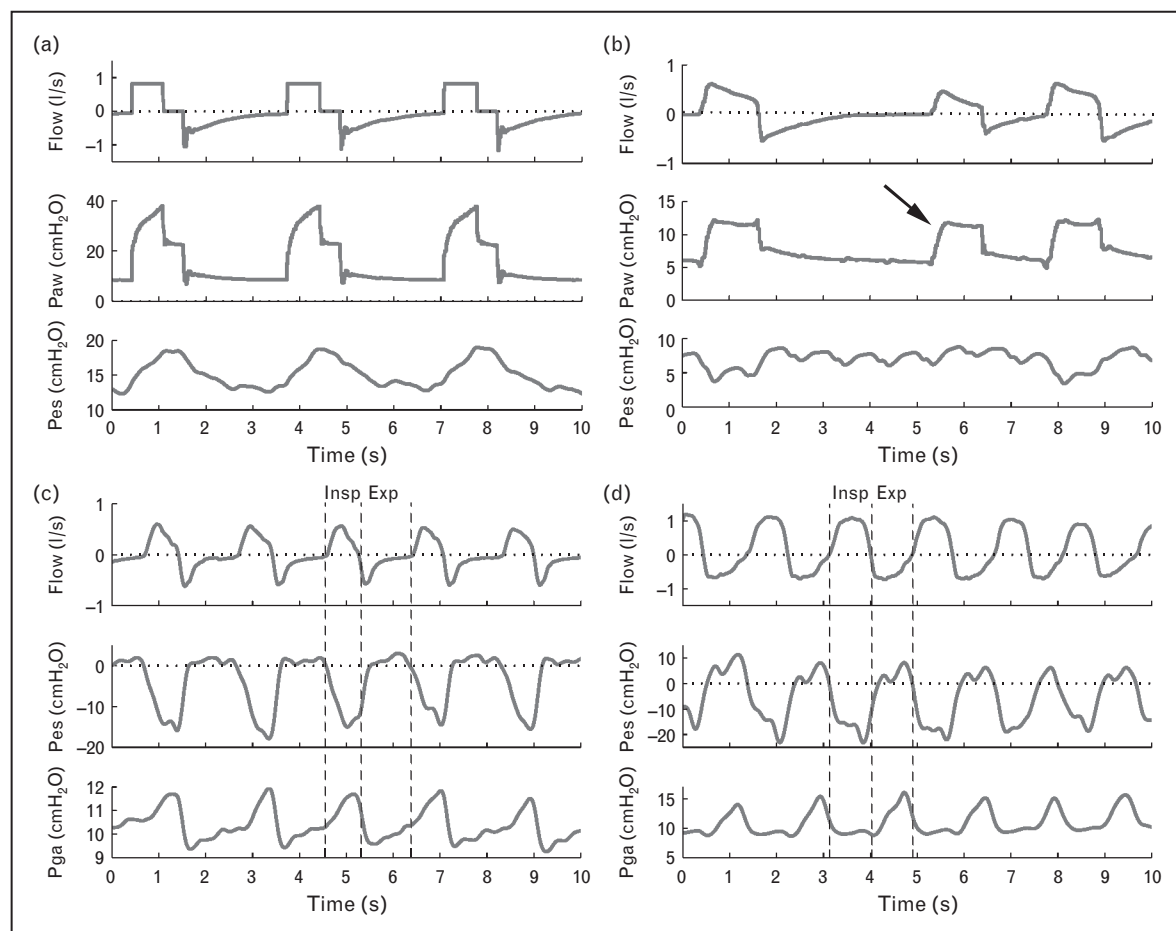


FIGURE 1. Monitoring of respiratory muscle function using esophageal pressure (P_{es}). Tracings of flow, airway pressure (P_{aw}), P_{es} and gastric pressure (P_{ga}) under different conditions. (a) Patient on controlled mechanical ventilation. P_{es} increases during mechanical inspiration. There is no decrease in P_{es} before mechanical inspiration, indicating absence of respiratory muscle activity. Note the perturbations in P_{es} resulting from cardiac activity. (b) Patient-ventilator asynchrony during pressure support ventilation; arrow indicates an autotriggered breath. Note the absence of a deflection in P_{es} in this breath, which is present in the other two breaths. (c) Weaning patient during a successful spontaneous breathing trial with T-piece, showing negative P_{es} and positive P_{ga} swings during inspiration. (d) Weaning patient during a failed spontaneous breathing trial with T-piece. Note the increase in P_{ga} during the expiratory phase to compensate for diaphragm weakness or high intrinsic positive end-expiratory pressure. Note that in this case, the decrease in P_{es} at the beginning of inspiration (e.g. the breath just after $T=3$ s) results from both relaxation of the abdominal muscles (note decrease in P_{ga}) and contraction of the diaphragm.

Diaphragm and accessory muscle electromyography

Electromyography (EMG) reflects the temporal and spatial summation of muscle action potentials. Characteristics of the EMG signal depend on the neural drive and muscle membrane characteristics. Diaphragm EMG can be acquired with surface or esophageal electrodes. The latter has been shown to be more reliable mostly because of reduced cross talk from other muscles. Diaphragm EMG has been used for research purposes for decades. More recently, diaphragm EMG acquired with esophageal electrodes (Edi catheter) is used clinically to control the ventilator during neurally adjusted ventilatory assist [15]. In this mode, the processed diaphragm EMG signal (EAdi) is available in real time as long as the EAdi catheter is connected to the ventilator. EAdi is suitable for monitoring of diaphragm activity under different clinical conditions (Fig. 2). A limitation is that this mode is available only on ventilators from

one company (Maquet Solna, Sweden). The amplitude of the EAdi signal reflects breathing effort during mechanical ventilation in patients with acute respiratory failure [16]. In general, reducing ventilator support will increase the amplitude of the EAdi signal (Fig. 2).

The commercially available EAdi catheter serves as a feeding tube also, and therefore EAdi monitoring does not impose an additional patient risk, despite its invasive nature. Alternatively, surface EMG can be used to detect electrical activity of the diaphragm and other respiratory muscles. Practical aspects including cross talk from other muscles, low signal-to-noise ratio in certain patients (obesity, edema) and impaired patient mobilization, however, limit routine use of surface EMG in clinical practice.

Although relatively simple EAdi parameters, such as peak activity, are available today for monitoring diaphragm muscle function, more advanced EAdi monitoring holds promise for the

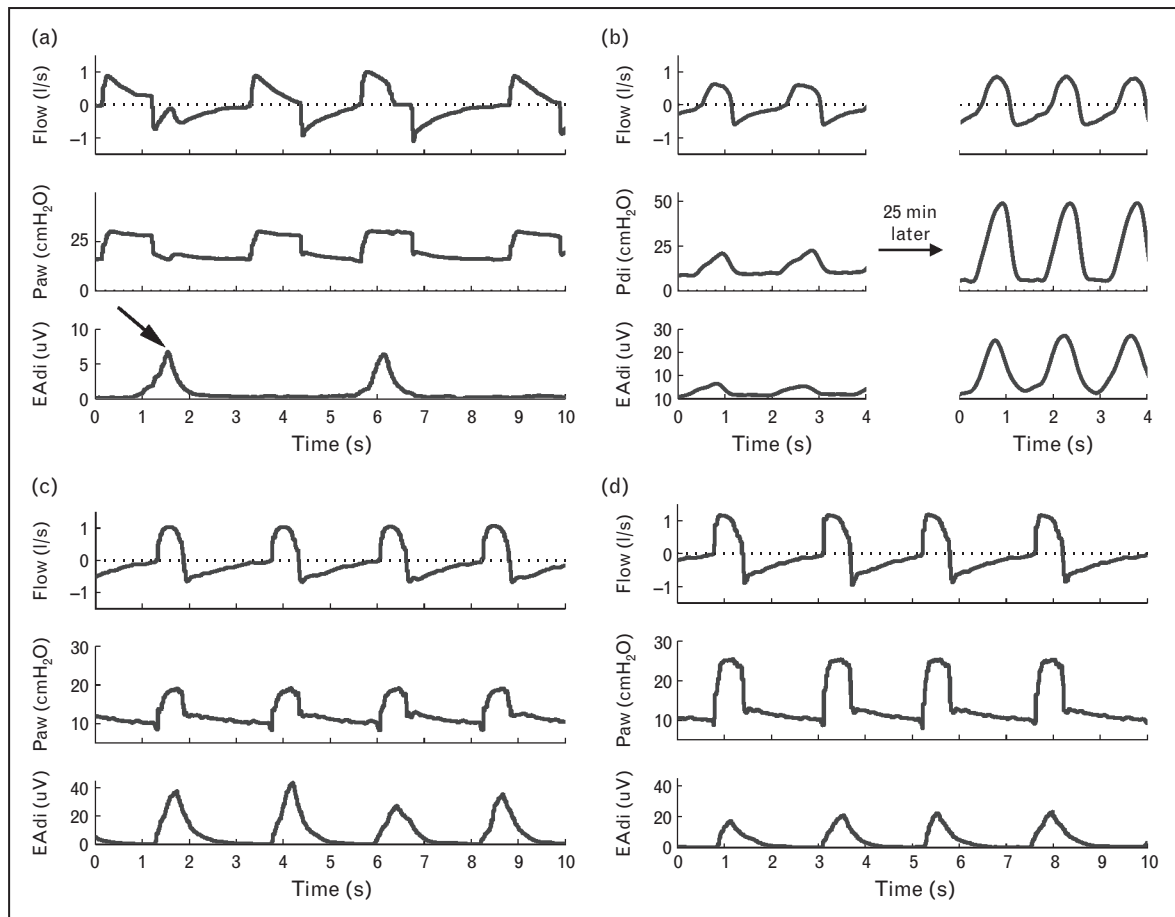


FIGURE 2. Monitoring diaphragm function using processed EMG. Tracings of flow, airway pressure (Paw), electrical activity of the diaphragm (EAdi) and transdiaphragmatic pressure (Pdi) under different conditions. (a) Patient-ventilator asynchrony during assist control ventilation. Arrow indicates a wasted effort following a machine-cycled breath. (b) Weaning patient during a failed spontaneous breathing trial with T-piece. Left panel shows tracings in first minute of the trial and right panel 25 min later. Note the increase in EAdi and Pdi. Subparts (c) and (d) represent same patient, ventilated with low (c) and high (d) pressure support. Note the decrease in EAdi resulting from a reduction in pressure support level. EMG, electromyography.

future. First, a computer algorithm has been developed that automatically quantifies asynchrony and dyssynchrony between patient and the ventilator using EAdi [17]. This tool is of potential interest, because it allows a breath-by-breath insight in patient–ventilator interaction. Second, power spectrum analysis can detect changes in the characteristics of the EMG signal that are compatible with certain type of muscle fatigue [18–20]. Third, during assisted mechanical ventilation, part of the work of breathing is delivered by the patient and part by the ventilator. Animal studies have shown that during neurally adjusted ventilatory assist, the EAdi can be used to calculate the percentage of the total work of breathing that is performed by the patient, the so-called patient–ventilator breath contribution [21]. Although these three examples are of interest, the benefits and feasibility should be tested before widespread use in patients.

Ultrasonography

Ultrasound is widely available, portable, noninvasive and easy to use, and therefore a popular tool in the ICU. It, however, is not suitable for continuous data acquisition and therefore in the gray zone between a monitoring tool and a diagnostic tool. Roughly, ultrasound is used to assess diaphragm thickness and movement. Thickness at the end of expiration can detect atrophy [22]. Measuring change in thickness between inspiration and expiration (thickening fraction) has been used to assess work of breathing [23]. Ultrasound is an excellent tool to assess diaphragm movement. Reference values are available for diaphragm displacement in healthy individuals [24]. Caution should be taken in evaluating movement of the diaphragm. The diaphragm moves caudally with active inspiration, but also passively during positive pressure ventilation. Simultaneous recording of airway pressure and diaphragm M-mode is helpful for the detection of wasted efforts. Also, trigger delay can be calculated if signals are displayed simultaneously [25]. Autotriggering may be harder to detect because, with inspiration, the diaphragm moves downward, even in the absence of muscle contraction.

CLINICAL APPLICATION OF RESPIRATORY MUSCLE MONITORING

Today, Pes (\pm Pga) and EAdi are probably the best tools to monitor respiratory muscle activity in ICU patients. Both techniques allow continuous and real-time tracking of respiratory muscle activity. They pose no additional risk to the patients, despite their invasive nature, assuming that the patient needs a nasogastric tube for feeding anyway. Ideally,

target values should be defined for respiratory muscle activity. The values are not available, neither for EAdi nor for Pes or Pdi. Moreover, the desired level of activity may change during ICU stay, depending on the clinical condition of the patient. This will be discussed below, and we have for clarity divided ICU stay in three phases, which of course may not be applicable to all of our patients.

Early phase

In patients with severe acute respiratory distress syndrome (ARDS) or severe hypercapnic exacerbation of chronic obstructive pulmonary disease (COPD), respiratory muscle activity may enhance lung injury [26]. In these patients, neuromuscular blockers may be used to inactivate the respiratory muscles [27]. Both EAdi and Pes monitoring are suitable to confirm the absence of respiratory muscle activity (Figs. 1 and 2). Absence of EAdi during inspiration virtually excludes diaphragm activation. Also, absence of deflection of Pes at the beginning of inspiration excludes activity of the respiratory muscles. Both techniques may be considered to titrate the dose of neuromuscular blockers accomplishing complete muscle relaxation and the lowest drug dose.

Recovery phase

Once the patient recovers from acute respiratory failure, assisted modes for ventilation are usually instituted. At this time, the focus of monitoring changes to the prevention of overassist and optimal synchrony between the respiratory muscles and the ventilator.

A rationale for using assisted ventilation is to limit the development of respiratory muscle atrophy because of disuse [4], and therefore overassist should be prevented. However, inadequate unloading will result in discomfort and may have adverse effects on the respiratory muscles [28]. Unfortunately, the optimal level of diaphragm muscle activity in ventilated patients is unknown. Therefore, a more pragmatic approach is reasonable. When EAdi is used to monitor diaphragm activity, electrical activity should be clearly visible with each ventilator assist (no overassist), but the patient should be adequately unloaded based on clinical characteristics. When using Pes as a monitoring tool, at least a decrease in pressure at the initiation of inspiration should be visible with all of the assisted breaths, while the patient is adequately unloaded from the clinical perspective. Note that the interpretation of these pressure signals may be complex, in particular when the patient uses expiratory muscles. In these patients, a drop in pressure at the initiation of

inspiration may result from contraction of the inspiratory muscles, relaxation of the expiratory muscles or both. This can be differentiated by simultaneous measurement of Pga, but makes monitoring more complex (Fig. 1d).

Patient-ventilator asynchrony is very common during assisted ventilation [29]. Both EAdi and Pes monitoring are suitable to monitor patient-ventilator asynchrony [9,30]. A limitation today is that no software is commercially available that tracks and quantifies asynchronies in real time. Sinderby *et al.* [17] recently developed and tested such an algorithm. The value of this monitor in clinical care needs to be established.

Weaning phase

In this phase, patients are subjected to weaning trials when the level of assist is acutely reduced. Besides continued monitoring for asynchronies, the effect of reduced assist on respiratory muscle performance can be monitored. Estimating patient effort during a weaning trial may help to predict success of extubation. Jubran *et al.* [13] demonstrated that repeated measurement of Pes swings is helpful in predicting weaning outcome. Moreover, detailed analysis of the Pes swings versus tidal volume allows calculation of the work of breathing and insight in the case of elevated work of breathing (Fig. 1b). As mentioned, interpretation of Pes in ventilated patients, or during a weaning trial, may be complex. Patients with imminent respiratory failure will recruit expiratory muscles, which will affect Pes independent from inspiratory muscle activity. The value of Pes monitoring in the weaning phase needs to be evaluated in future studies.

More recently, EAdi has been used to monitor diaphragm activity during weaning trials. Liu and colleagues demonstrated that EAdi during a weaning trial (CPAP 5 cmH₂O) was significantly higher in weaning failure patients compared with that in weaning success patients. More sophisticated indices, such as neuroventilatory efficiency (EAdi/tidal volume) and neuromechanical efficiency (EAdi/Pdi), were lower in weaning failure patients compared with those in weaning success patients. It should be noted that these are only preliminary studies, but show promise for more intensive monitoring in the near future.

CLINICAL RELEVANCE OF RESPIRATORY MUSCLE MONITORING

The ultimate goal of monitoring is to improve outcome. Monitoring of the respiratory muscles is in its

infancy, and no clinical trials have been conducted to test the effects of respiratory muscle monitoring on clinically relevant outcome parameters. Although solid evidence that respiratory muscle monitoring improves outcome (and is cost-effective) would be welcome, it is extremely challenging to demonstrate the clinical benefit of any monitoring technique [31]. Until then, a physiological and clinical judgment is important for the decision to apply any monitoring of any vital function, including the respiratory muscles. In our opinion, it is reasonable to consider monitoring in patients with the highest likelihood of developing muscle weakness in the ICU and in patients with a high likelihood of asynchrony. Supinski and Ann Callahan [8] reported that infection is a major risk factor for the development of ICU-acquired weakness. Patients with preexistent muscle dysfunction may be prone to the adverse effects of critical illness on the respiratory muscles and are more likely to exhibit asynchrony. Accordingly, in our opinion, respiratory muscle monitoring should be considered in the following patient categories: septic shock, severe ARDS and severe exacerbation of COPD.

CONCLUSION

Every clinician will use monitoring tools to track changes in physiological function and guide management decisions in patients with acute circulatory failure. It is therefore surprising that in the case of severe respiratory failure, no tools are used to monitor respiratory muscle function. It has been shown that critical illness and ICU treatment may adversely affect the respiratory muscles. Therefore, clinicians should more often consider the use of monitoring tools to evaluate respiratory muscle activity. Both diaphragm EMG and Pes can be used for monitoring. Scientists and industry should work together to improve techniques for monitoring the respiratory muscles in our patients.

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