Core Knowledge in Critical Care Medicine

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Wolfgang Krüger

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Chapter 1
Mechanical Ventilation

1.1 Acute Respiratory Failure

Acute respiratory failure (ARF) is defined as the inability of the respiratory system to meet the oxygenation, ventilatory, or metabolic requirements of the patient [1].

Most authors divide respiratory failure based on the two gas exchange functions, oxygenation and elimination of carbon dioxide. Either, "only" oxygen replenishment may be compromised or a joint disruption occurs [2, 3]:

I. Hypoxaemic respiratory failure
II. Hypercapnic respiratory failure

Hypoxaemic respiratory failure refers to the failure of the lungs to oxygenate mixed venous blood sufficiently, P_aO_2 <60 mmHg- [4, 5], while hypercapnic respiratory failure indicates a blunted elimination of carbon dioxide resulting in respiratory acidaemia with a P_aCO_2 >50 mmHg in the presence of hypoxaemia [5–7].

Hypercapnic respiratory failure is called ventilatory failure as well [6], highlighting that the ventilatory part of the respiratory system – the "pump function" of the respiratory apparatus – has failed, mainly due to ventilatory muscle fatigue, rather than to the gas exchange element [5].

As such, hypercapnia is a hallmark of ventilatory failure [5, 8], and an acutely decompensated ventilatory failure is characterized by a respiratory acidosis (pH <7.35) in the presence of hypercapnia [5].

Accordingly, the majority of authors classify respiratory failure into two subtypes [7, 9, 10], although others may distinguish four types [11, 12]:

Type 1: Hypoxaemic respiratory failure

Shunting and a ventilation–perfusion mismatch (V/Q mismatch) are the most common underlying pathophysiological mechanisms causing hypoxaemia [10, 13, 14]. While V/Q mismatch will easily respond to oxygen delivery (chronic obstructive pulmonary disease is a typical example [11]), hypoxaemia due to shunting will persist even if oxygen is supplied [11, 15]. Pulmonary shunting can be interpreted as an extreme form of V/Q mismatch [15] which occurs in the

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setting of alveolar hypoventilation or alveolar collapse related to atelectasis and/or alveolar flooding from infection, blood or fluid [16]. Typical examples are cardiogenic pulmonary oedema, non-cardiogenic pulmonary oedema (ARDS), pneumonia, lung haemorrhage, and atelectasis [5, 11, 17]. Other conditions which may produce hypoxaemic respiratory failure include alveolar hypoventilation due to high altitude (low FiO_2), diffusion abnormalities and low mixed venous oxygen content subsequent to increased peripheral uptake [10, 13, 14].

Type 2: Ventilatory, hypercapnic respiratory failure

Type 2 respiratory failure is attributed to alveolar hypoventilation as found in (a) central nervous system disturbance, e.g. anaesthesia, head injury, drug overdose;(b) neuromuscular diseases, e.g. myasthenia gravis, Guillain–Barre syndrome, spinal cord diseases, myopathies;(c) elevated breathing workload, e.g. COPD, asthma, pulmonary fibrosis; and (d) increased dead space, e.g. pulmonary embolism, hypovolaemia, poor cardiac output, alveolar distension and/or increased CO_2 production as in fever, sepsis or burns trauma [10, 11].

Respiratory acidosis in the setting of chronic ventilatory failure must be considered a potentially life-threatening situation, and early mechanically ventilatory support is warranted [5].

Some authors additionally discriminate two further types:

Type 3: Perioperative ventilatory failure

This is actually a subtype of type 1 and is especially common in the postoperative phase. The main pathophysiology is atelectasis resulting from decreased functional residual capacity (FRC), anaesthesia, upper abdominal incision, airway secretions, supine position, obesity and ascites [11].

Type 4: Respiratory failure in conditions of shock

Hypoperfusion may affect respiration attributed to either increased demand or compromised delivery, leading to ARF [11, 12]. In addition, the central respiratory drive may be blunted [11].

Accordingly, a wide variety of etiological conditions may cause ARF, often not directly affecting the lung tissue [7].

Causes of type I respiratory failure include [5, 17]:

- ARDS
- Acute asthma
- Pulmonary fibrosis
- Pneumonia
- Pulmonary embolism
- Pneumothorax
- Pulmonary oedema
- COPD

Conditions such as pneumothorax, asthma or particularly COPD may present initially as type I respiratory failure but become complicated by developing hypercapnia, related to worsening ventilation–perfusion mismatch and/or increasing work of breathing resulting in exhaustion of the respiratory muscles [5]. The latter is referred to as *ventilatory failure* [5, 6] (see above).

Causes of type II respiratory failure include [5, 17]:

- COPD
- Kyphoscoliosis
- Obstructive sleep apnoea
- Acute severe asthma
- Abdominal distension (ascites, blood, peritonitis, pancreatitis, etc.)
- Morbid obesity resulting in obesity hypoventilation syndrome
- Chest wall trauma, e.g. flail chest or pneumothorax
- Central nervous system with depression of central respiratory drive
  - Coma
  - Raised intracranial pressure
  - Drugs, i.e. opioids, sedative
- Neuromuscular diseases
  - Peripheral nervous system, e.g. Guillain–Barre syndrome, critical illness polyneuropathy
  - Neuromuscular junction, i.e. myasthenia gravis, muscle relaxants, organophosphate poisoning
  - Myopathy, e.g. muscular dystrophy
  - Cervical cord lesion, e.g. trauma, tumour, etc.

1.2 Epidemiology

A review by Esteban [18] revealed that the indications for positive pressure mechanical ventilation (PPMV) include:

- Acute respiratory failure 66 %
- Coma 15 %
- Acute exacerbation of COPD 13 %
- Neuromuscular disorders 5 %

This was largely confirmed in other surveys [19, 20], however all of these studies were also performed by Esteban and colleagues. Acute respiratory failure may be caused by a number of different disease entities such as pneumonia, postoperative conditions, acute heart failure, ARDS and sepsis being the most frequent ones (between 10 and 18 % each) [18–20]. Thirty three percent [20] to 46 % [21] of all patients admitted to an ICU need PPMV for more than 12–24 h and the overall median duration of PPMV is reported to be 3 days [20]. However, a wide range exists: from 2 days in postoperative cases [22], over 4 days in COPD [20], up to 11 days in pneumonia [23] and 6–15 days in ALI/ARDS [20]. Only a very small number (3 %) needed more than 3 weeks of ventilatory support [20].

Ventilator-associated pneumonia (VAP) occurs in 8–28 % of cases [24], and the incidence increases with the duration of PPMV [25]. Interestingly, the risk rate

lowers the longer the patient is ventilated, as shown by Cook [26], with the risk rates of 3% on day 5, of 2% day 10 and of 1% on day 15. However, the cumulative risk is estimated to be 7 % at 10 days and 19 % at 20 days [27]. However, differences in the definitions require some caution when generalizing this data.

Published mortality rates vary widely [28, 29], and it is important to note that ventilator settings have changed fundamentally since the implementation of lung protective ventilation in 2000, specifically regarding rates of acute lung injury/acute respiratory distress syndrome (ALI/ARDS) [30]. In unselected populations of PPMV patients, the reported mortality rates range from 64 % in an older (1993) study [31] to 39 % in a publication in 2002 [20]. Ideally therefore, when comparing ventilator-related mortality rates, the disease-specific rates should be considered.

1.3 Ventilator Modes Nomenclature

There is a profusion of terms used to describe ventilator modes which may be inconsistent and confusing, and multiple different names may be used to describe the same function [32, 33]. However, there are a number of main general principles.

The mode of mechanical ventilation refers to the method of inspiratory support [34] and comprises three components: (a) the control variable which may be volume or pressure controlled, or dual switching from one mode to the other during one breath may be permitted; (b) the breath sequence which may be continuous mandatory, intermittent mandatory or spontaneous; and (c) the targeting scheme, feedback or type of control mechanism(s) referring to the programmed ventilator target settings, i.e. respiratory rate, tidal volume, minute volume or combined targets [32, 33]. The new generation of ventilators are equipped with adaptive features and use modelled algorithms which calculate how to achieve set goals. However, it is not possible to control both pressure and volume simultaneously [33, 35].

Based on these principles, eight ventilation modes can be identified [32, 36]:

Control variable	Breath sequence	Acronym
Volume	Continuous mandatory ventilation	VC – CMV (IPPV)
	Intermittent mandatory ventilation	VC – IMV
Pressure	Continuous mandatory ventilation	PC – CMV (IPPV)
	Intermittent mandatory ventilation	PC – IMV
	Continuous spontaneous ventilation	PC – CSV (PSV/ASB)
Dual	Continuous mandatory ventilation	DC – CMV (CMV, pressure limited)
	Intermittent mandatory ventilation	DC – IMV (IMV, pressure limited)
	Continuous spontaneous ventilation	DC – CSV (CSV, pressure limited)

PC pressure control, *VC* volume control, *DC* dual control, *IPPV* intermittent positive pressure ventilation, *PSV* pressure support ventilation, *ASB* assisted spontaneous breathing

Pressure support ventilation (PSV) or just pressure support (PS) amplifies the patient's own respiratory efforts on patient-initiated breaths [37, 38]. With contemporary ventilators, triggering requires the patient to create a small negative inspiratory flow of −1 to −2 cm H_2O [39] which will, if achieved, lead to the initiation of the set support pressure [40]. Compared to conventional pressure triggering, flow triggering

probably decreases the work of breathing [41, 42] and minimizes the risk of development of auto-PEEP/gas trapping inherent to the ventilator settings [43, 44].

Synchronized intermittent mandatory ventilation (SIMV), or now just shortened to IMV [32], refers to a volume- or pressure-controlled mode where the patient is able to trigger set mandatory breaths. This is allowed to occur only during a limited, short phase at the end of expiration prior to the next mandatory breath being delivered, and in addition to a set rate of breaths per minute supplied by the ventilator (whether patient triggered or not), the patient may spontaneously activate further breaths. These will usually be pressure supported [32, 36, 40], in order to ensure an adequate tidal volume which otherwise may vary according to the patient's respiratory muscle capability [40].

The term dual control was coined by Branson [45]to describe the technical ability to switch from one control mode to the other during a single breath cycle, i.e. starting with volume control in order to achieve a set tidal volume (V_T) target but limiting the pressure automatically generated to meet that V_T [32]. The same intention is also known as volume target pressure control which, in line with the results from the ARDSnet group in 2000 [30], limits the pressure to match the lung protective ventilation settings [40]. In recent years the dual or adaptive pressure-control algorithms have become widely available and combine pressure-limiting and volume-cycling features. This is achieved either by regulating the pressure in a volume-controlled mode (PRVC) or by assuring a specific volume in a pressure-controlled manner. It is physically achieved by affecting the flow delivered over a variable time, and the pressure is held after flow has stopped [46]. However, this approach has its limits; a minimum V_T is guaranteed but will not be constant because V_T depends on a complex relationship between respiratory compliance, airway resistance and patient effort and the ventilator is unable to distinguish between changes in lung mechanical properties and improved patient effort [46].

1.4 Volume-Controlled (VC) Versus Pressure-Controlled (PC) Ventilation

Positive pressure mechanical ventilation (PPMV) either in VC or PC mode replaces the physiological negative pressure respiration by the exact opposite mechanism [40]. Indeed, negative-pressure ventilatory support was used in at the advent of mechanical ventilation, but following the results observed during the polio epidemics in the 1950s, where those patients ventilated with negative-pressure generating mechanical ventilators had worse outcomes compared to those treated with PPMV, the technology shifted completely towards the positive pressure variant [47, 48].

Mechanical ventilatory support mainly increases lung volume that decreases in various disease states due to altered lung mechanics, namely, diminished lung and/or chest wall compliance and elevated airway resistance. This considerably supports the work of breathing by unloading the exhausted respiratory muscles, allowing them to recover, and thus improves pulmonary gas exchange, the latter further improved by a revised ventilation–perfusion mismatch [49–52].

Volume-controlled ventilation is the most frequently used mode worldwide as physicians are more familiar with this type of ventilatory support rather than with

pressure-controlled [18]. This may also represent a desire to safeguard tidal and minute volumes which have traditionally been considered the most important target of respiratory support, and high V_T may avoid formation of atelectasis by avoiding alveolar hypoventilation [53]. In VC, the tidal volume set is delivered; however, the pressure necessary to reach the desired V_T will vary and may exceed our limits of peak and plateau pressure [35, 54, 55]. In contrast, in PC mode the pressure set will definitely be generated, but the consecutive tidal volumes will vary as it follows a complex function (see below) largely determined by the respiratory mechanics [54, 55]. The pressure level has to be adjusted if compliance or resistance change, in order to avoid too low or too high V_Ts which may risk atelectasis or over-distension, respectively [46]. Although a large body of literature concludes that no significant differences exist between PC and basic modes of ventilation, in terms of outcome, duration of ventilation or ICU and hospital stay exist [56–58], PC may still have some advantages. Even in VC, the maximal pressures applied need to be limited as there is good evidence that plateau pressures higher than 26–28 cm H_2O [59–61] or a peak inspiratory pressure (PIP) higher than 30–35 cm H_2O [53, 62] may have detrimental effects and should be avoided [54]. Moreover, in PC mode a more favourable pressure distribution and dissemination of the airway pressures including a significant reduction in peak pressure are found compared to VC [63, 64]. Decelerating inspiratory flow patterns are applicable in PC but not in VC (only constant patterns) and are associated with improved air distribution in the lungs which have heterogeneous mechanical properties [65–67] and will facilitate gentle and tissue preserving airway pressure and air distribution conditions. Decelerating inspiratory flow is shown to be especially of value in lungs with poor compliance [40, 68]. At the least, PC may be more comfortable for patients due to a better interaction between patient and ventilator, particularly in obstructive lung diseases [69].

In PC the main disadvantage is potential hypoventilation due to varying lung and chest wall mechanics which allows variations in V_T, whereas in VC the high pressures applied may be harmful, VC cannot compensate for leaks [54, 69] and the fixed flow may lead to patient–ventilator dyssynchrony [46]. However, VC will control the ventilation, may better manage hypoventilation during the first phase of respiratory failure and exhibits the lowest degree of hyperinflation if high inspiratory flows are applied and long expiratory times allowed [69].

In order to better synchronize patient and ventilator, two very similar pressure-controlled methods of ventilation have been developed, the so-called bilevel, BiPAP or BiLevel ventilation, and airway pressure release ventilation, APRV. Biphasic positive airway pressure (BiPAP, BiLevel) and airway pressure release ventilation are modified pressure-controlled modes [40, 70]. APRV combines repetitive application of a constant high positive airway pressure (P_{HIGH} or high PEEP level), generating a tidal volume with intermittent pressure releases to a lower pressure level (P_{LOW} or low PEEP level) causing expiration [71]. As the inspiratory time is kept very prolonged there is only a short exhalation time in this pressure-controlled (IMV) ventilatory mode, potentially and intentionally creating auto-PEEP [70]. However, spontaneous breathing is possible at any time, making patient–ventilator interaction much more comfortable [32, 72]. Biphasic positive airway pressure

ventilation (BiPAP) also allows, in principle, for unrestricted spontaneous ventilation (inspiration as well as expiration) at any time during the respiratory cycle, resulting in reduced sedation requirements and promoting weaning [54, 70]. This mode also applies two different pressure levels, P_{HIGH} and P_{LOW}, and is conceptually equal to AVPR [70] with the exception that the duration of the lower pressure level is far longer than in AVPR where it is by convention less than 1.5 s [33] and that BiPAP is supportive in spontaneous breaths [70]. AVPR represents a form of inversed ratio ventilation (IVR) which means that the inspiratory time is extremely prolonged in order to strongly support oxygen replenishment [33]. In BiPAP, I:E ratio can be determined by the physician and generally any ratio is available (e.g. inversed, 1:1, up to 1:4 [5]) [33]. In both types, the lower pressure level applies PEEP while with the change to the higher level, air will be inflated [33, 70]. Unfortunately, in AVPR the inversed ratio which may be necessary in severe hypoxaemia requires sedation or even paralysis [54]. However, as both techniques significantly improve oxygenation, attributed to alveolar recruitment and improved ventilation–perfusion matching [73], and as the more moderate settings in BiPAP allow spontaneous breathing, they are commonly applied in patients with hypoxaemic respiratory failure and BiPAP may routinely be the initial ventilation mode. Recommended settings are an initial fairly high-pressure level of 12–15 cm H_2O above set PEEP [74]. The potential for spontaneous breathing at any time is of very high value as it not only facilitates patient–ventilator interaction and synchrony but helps to avoid respiratory muscle fatigue and longer-term respirator dependency of which the main cause is diaphragm dysfunction and fatigue [75–77].

CPAP is a PC mode delivering a constant level of positive pressure throughout the respiratory cycle [40]. It may be applied in a broad range of causes of respiratory failure as by increasing mean airway pressure, collapsed and hypoventilated lung units will be reinflated and kept open during expiration with consecutive increase in functional residual capacity (FRC). This results in improved gas exchange and oxygenation [78] and so this technique is particularly indicated in hypoxaemic respiratory failure [40]. Moreover, as CPAP will improve the lung compliance as well, it reduces the work of breathing and thus may avert the development of overt muscle or ventilatory failure [79–81].

1.5 Indications for Intubation and Mechanical Ventilation

The decision to intubate a patient is a complex assessment process requiring the consideration and integration of numerous aspects and facts, but remains largely a clinical judgement, and in daily practice is essentially concurrent with the determination to apply PPMV [5, 17, 35, 82–84].

A review by Esteban revealed that the indications for PPMV include [18]:

- Acute respiratory failure 66 %
- Coma 15 %
- Acute exacerbation of COPD 13 %

- Neuromuscular disorders 5 %

Frequently designated/specified indications for PPMV [85]:

- Acute respiratory arrest
- Apnoea and impending respiratory arrest
- Acute hypoxaemic respiratory failure
- Coma and acute neuromuscular diseases
- Acute exacerbation of COPD
- Heart failure and cardiogenic shock
- Cardiac arrest
- Acute severe asthma
- Acute brain injury
- Flail chest

The physiological consequences of a sustained pH >7.65 or <7.10 are considered dangerous in itself if not quickly reversible and thus may require mechanical ventilation [35]. Within this range from pH 7.1 to 7.65, the clinical condition is seminal in how to approach the patient [86]. Some indicators in the setting of respiratory dysfunction and distress which support the initiation of PPMV are [50]:

Respiratory rate	>35/min
Tidal volume, spontaneously	<5 ml/kg
Vital capacity	<10 ml/kg
Rise in P_aCO_2 from baseline	>10 mmHg
Negative inspiratory force	<−25 cm H_2O
P_aO_2 with supplemented	O_2 <55 mmHg
Alveolar–arterial gradient (on $FiO_2 = 1.0$)	>450 mmHg
P_aO_2/P_AO_2 ratio	<0.15
GCS	<8

A GCS less than eight comes with the risk of not protecting the airway. Intubation should generally be considered and may be mandatory in head injuries [87]; however, a GCS <8 is otherwise not an absolute indication for intubation [88].

Aside from the clinical assessment, other features may help in making the decision whether to intubate or not [17]:

- Initiation of PPMV necessary and needs facilitation
- Protection from aspiration, particularly in patients not able to protect their airway, which is generally the case in altered mental status as indicated by a GCS <8
- Facilitation of tracheobronchial suction
- Relief of upper airway obstruction

Further, specific indications for ventilatory support and/or intubation are depicted in the paragraphs on ventilation in patients suffering from non-ARDS ventilator failure, COPD, asthma and the separate chapter on ALI/ARDS.

1.6 Patient–Ventilator Interaction

PPMV is applied to patients struggling with substantial respiratory difficulties in order to largely unload the respiratory muscles by taking over or sharing the work of breathing, facilitating lung inflation and gas exchange, thus reducing dyspnoea [89–91]. Spontaneous breaths and breathing efforts may be initially replaced by the ventilator, but as passive mechanical ventilation will lead to considerable respiratory muscle dysfunction and atrophy [92, 93], its timely withdrawal is of pivotal importance [89]. In order to facilitate this, the ventilator actions/responses must synchronize with patients' spontaneous breathing efforts and demands [89–91, 94, 95].

When considering why a patient is combating the ventilators, multiple factors may be contributing; these include underlying lung functional abnormalities, the ventilator settings set by the clinician, the specific ventilator functions, the patient–ventilator interface, and not at least the patients' own airway responses [89, 91, 96, 97]. NIV intolerance is most clearly related to asynchrony [94]. Of particular importance and interest are trigger asynchronies [89, 90, 94, 95], reported to be found in up to 58 % of all patients [94]. Asynchronies (patient–ventilator interactions) in general are associated with adverse outcomes, prolonged duration of PPMV and higher rate of tracheostomy [98–100] due to ineffective ventilation with increased work of breathing, lung over-distension, impaired gas exchange and patient discomfort [89]. Anxiety and dyspnoea often result from dyssynchronous interactions [90]. Particularly predisposed to mismatch between patients' request (ventilatory drive and muscular effort) and the machine's reply (airflow and pressure delivered) are patients with COPD and ALI/ARDS [89].

Trigger asynchronies comprise ineffective trigger efforts, auto-triggering, delayed triggering and premature and delayed release of flow and pressure–volume [89, 91] with the most common problem being ineffective or wasted efforts [101]. A trigger effort, in the vast majority occurring during the expiratory period, indicated by an abrupt decrease in airway pressure of >0.5 cm H_2O is ineffective if not resulting in an assisted breath from the ventilator (if the trigger occurs during expiration, accompanied by a decrease expiratory flow) [99]. Ineffective efforts, also known as ineffective triggering, untriggered breaths or trigger asynchrony, may occur as well during inspiration, indicated by an abrupt increase in inspiratory flow (in PC mode) or transient abrupt decrease in airway pressure (VC mode) [89, 95]. Dynamic hyperinflation, limited respiratory drive, weakness of respiratory muscles and insensitive trigger settings are causally underlying ineffective efforts [102]. Since resolving a dys-synchrony in one area often facilitates other adverse interactions as well [90], the most common problem is discussed in detail below.

Although the specific analysis of disadvantageous patient–ventilator interactions and how to tackle them have been more and more recognized in recent years, the first systematic approach of how to analyse and manage trigger asynchronies has been recently done by Sassoon [95]. In brief, low PEEP (5 cm H_2O are very common) should be applied, but adjusted in case of measured or suggested intrinsic PEEP (PEEPi) to 75–80 % of PEEPi as with Nava [103]. If there is still an asynchrony

index of >10 %, increase PEEP by steps of 1 cm H_2O up to max 8 cm H_2O. If still wasted efforts are present, adjust V_T to 6–8 ml/kg PBW [104]. Thereafter, increases in inspiratory flow rate (VC) or pressure (PC) are recommended. Further steps and details, see Fig. 1.1 below:

[Def asynchrony index (AI) = number of wasted efforts/number of wasted efforts plus triggered breaths during a period of 2 min [105] in percent [99]]

Keep in mind that some degree of asynchrony may always be present [95].

1.7 Basics of Respiratory Physiology and Pathophysiological Issues

To breathe and thus inflate the lungs, a pressure gradient between the nose/mouth (atmosphere) and the lungs (alveoli) is needed as air, like fluid, moves from the higher pressure level towards the lower one [106, 107]. During inspiration the contraction of the respiratory muscles, diaphragm and external intercostal muscles enlarges the thoracic cage. Due to the (elastic) recoil properties of the lungs, adhered to the chest wall by a thin layer of fluid, the enlarging thoracic cavity generates a negative intrapleural pressure which is accompanied by a subatmospheric, negative alveolar pressure, establishing a pressure gradient within the airways, called the distending or transpulmonary pressure [106, 108, 109]. Mathematically this distending or transpulmonary pressure (gradient) being the driving force of airflow can be described and is defined by

$$P_{TRANS} = P_{AL} - P_{PL} \left(\text{formula A}\right)$$

with P_{AL} being the pressure within the alveoli, and P_{PL} represents the pressure in the intrapleural space [106, 108, 110]. In mechanically ventilated patients, the airway pressure (P_{AW}) can be measured and equals alveolar pressure (P_{AL}) if there is no airflow [111, 112]. This is usually determined at end inspiration, as the end-inspiratory pressure is considered as being the most critical one since it distends the alveoli/alveolar units [113], but is otherwise influenced by lung and chest specific factors and properties

Fig. 1.1 Algorithm to improve patient–ventilator synchrony (With permission from Sassoon [95]). Start up to fine-tune PEEP as depicted. If $PEEP_i$ (intrinsic PEEP) cannot be measured or is ≤5 cm H_2O, go ahead with PEEP of 5 cm H_2O! With persisting asynchrony index (number of wasted efforts/number of wasted efforts + triggered breaths during a period of 2 min [%]) >10 %, increase applied PEEP by 1 cm H_2O steps up to a max of 8 cm H_2O, if measurable $PEEP_i$ apply 75–85 % of that. If after PEEP adjustment still a relevant asynchrony (asynchrony index >10 %) remains, adopt V_T: 6–8 ml/kg IBW. With ongoing asynchrony, increase respiratory flow rate in case of VCV or pressurization rate if the patient is on PCV. In the end, in case of time-cycled pressure target settings decrease inspiratory time, while in pressure support-ventilation, adjustment of the flow-cycling threshold is recommended: upward in case of prolonged expiration, otherwise downward