Editorial

The BREATHE-appeal: harmonize interaction between patient and ventilator!

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The development of the 'art' and science of mechanical ventilation (MV) in the 1950s was an important landmark in intensive care medicine. Modern intensive care is characterized by a high-level armamentarium of temporary replacement techniques for (nearly) all failing organ systems, thus improving the prognosis for many critically ill patients. In MV, however, there was a dolorous learning curve leading from disastrous controlled ventilation modes with high tidal volumes to modern lung-protective strategies. In acute respiratory distress syndrome (ARDS), which celebrates its 50th anniversary next year, such a learning curve was elegantly and exemplarily demonstrated by Slutsky *et al.* (1).

From the beginning of the era of artificial ventilation, it took a long time to accept that the major goal of MV is to withdraw it as soon as possible. That is because the negative side effects and 'collateral damage' of artificial airways and MV [deep sedation, ventilation-associated pneumonia, ventilation-induced lung injury, muscle weakness (2,3)] were identified as important factors in the impairment of prognosis in critically ill patients. In ARDS patients, it was shown that the early period of the severe lung injury is characterized as a most 'vulnerable' phase, and all measures for lung protection [protective ventilation, positioning, neuro-muscular relaxation, advanced anti-infective management (4)] are good investments in a favourable outcome. Consequently, the preferred mode for MV in early ARDS is controlled ventilation with low tidal volume and adequate positive end-expiratory airway pressure (PEEP) in combination with deep sedation aimed at protecting the lung and giving the parenchyma 'time to heal'. Interestingly, it has been demonstrated in recent years that controlled MV—for example, the volume-controlled assist-control (AC) mode in association with deep sedation—only apparently ensures 'harmony' between patient and ventilator. Quite the opposite, patient-ventilator dyssynchrony (PVD), is the reality even in deeply sedated patients—although this is not visible and often clinically not recognized. Meanwhile, the pathophysiology of PVD has been investigated in detail (5): during the acute phase of ARDS, the suppression of the spontaneous respiratory drive may be required, and controlled MV should have the sole control over respiratory rate and minute ventilation. But in both the controlled and assist-controlled modes, it frequently occurs that the patient's respiratory factors (inspiratory muscle pressure, neural and mechanical timing, respiratory system mechanics) are not matched by the ventilator breath-delivery patterns, which results in dyssynchrony. PVD can be identified as trigger dyssynchrony (patient is not able to trigger a ventilator cycle for several reasons), flow dyssynchrony (ventilator flow is inadequate to meet patient's demands), and cycle dyssynchrony (inspiratory signal is different between patient and ventilator; double-triggering may be a result). The

Table 1 Different types of patient-ventilator dyssynchrony

Type	Mechanism
Delayed triggering	Insensitive or false setting of trigger level
Ineffective efforts	Trigger asynchrony: insensitive trigger setting, untriggered breaths
Double-triggering	2 consecutive inspirations with an interval of <0.5 mean inspiratory time, "breath-stacking"
Auto-triggering	Unscheduled machine delivered breath without patient effort: triggering sensor too sensitive, presence of water in the circuit, vigorous cardiac oscillations
Delayed cycling	Ventilator inspiratory time 2× > patient's demand
Premature cycling	Ventilator inspiratory time < patient's demand
Flow asynchrony	Mismatch between delivered flow and patient's demand: inadequate low flow: slow and concave rise to peak pressure—too high flow: very fast rise to peak pressure (mimicking pressure control)

different types of PVD are presented in *Table 1*.

Meanwhile, PVD has been identified as a significant and potentially harmful fact in MV. It can cause an increase in the work of breathing, leading to ventilator muscle overload. More importantly, it might counteract lung-protective ventilation strategies. In a systematic review, Epstein *et al.* analysed the existing data on the prevalence of PVD (6). The conclusion was that the interaction between patient and ventilator is frequently suboptimal and that PVD is common. In the analysed studies, substantial dyssynchrony, defined as ≥10% of untriggered breaths, ranged from 30% of ARDS patients to 100% of patients suffering from chronic obstructive pulmonary disease (COPD). In most studies, the analysis and interpretation of bedside assessed waveforms was the tool used to identify dyssynchronies (7).

In an important recent study by Beitler *et al.* (8), the incidence and effects of PVD in 33 patients suffering from ARDS (90% moderate to severe ARDS, as per the Berlin definition) receiving volume-preset AC ventilation were analysed in a breath-by-breath record. The special interest of the authors was in the amount and possible under-recognition of breath-stacking dyssynchrony (BSD), which occurs when consecutive machine inspiratory cycles do not allow complete exhalation between them due to close succession of the cycles. In the study, airway flow and pressure were recorded continuously for up to 72 hrs and the flow-time waveform was integrated to calculate breath-by-breath tidal volume. For further characterization of BSD, the authors created five domains: ventilator cycling, interval expiratory volume, cumulative inspiratory volume, expiratory time, and inspiratory time (the BREATHE criteria). The most important results of this sophistically performed and clinically relevant study are as follows:

- The frequency of BSD, assessed by the BREATHE criteria, ranged from 7–59 breaths/h with a large variability between patients, and a substantial in-patient variation over time was observed (peak median BSD frequency =168 breath/h), although patients were 'adequately' sedated [Richmond Agitation and Sedation Score (RASS) between −4 and −1]. A clinically relevant BSD frequency (≥60 breath/h) was recorded during 18% (1–37%) of all documented hours;
- The BSD-associated tidal volume was 11.3 mL/kg (9.7–13.3 mL/kg) predicted body weight, which is nearly double the preset tidal volume of 6.3 mL/kg;
- The BREATHE-associated records detected significantly more BSD and more non-protective tidal volume (≥2 mL/kg than preset) in comparison with a visual waveform inspection: the automatically generated analysis of the incidence and quality of BSD was superior to the other existing criteria for the assessment of dyssynchrony;
- The application of neuromuscular blocking agents in ten study patients eliminated the BSD almost completely.

Which conclusions and consequences can be drawn from the study of Beitler *et al.*? First and most important, MV in a controlled mode with low tidal volume for the sedated patient is not a 'guarantee' for true lung protection: BSD and exposure to 'occult' high tidal volumes are common, and they may harm the patient and worsen the outcome. For the clinician, 'in-mind realization' and monitoring of dyssynchrony by frequent observations of the bedside waveforms could be a first step, but in future, we need automated recording and warning systems. Second, can we avoid or reduce the incidence of BSDs by changing our

ventilation and/or sedation practice? Recently, Chanques *et al.* (9) performed an intervention study in patients with documented severe breath-stacking asynchrony. The interventions were the increase of sedation or analgesia, or the ventilator adjustment. The change in ventilator settings was associated with a significant decrease of the asynchrony index compared to the increase of sedation or analgesia, which did not reduce asynchrony markedly. The authors concluded that the adaptation of the ventilator to the patient's breathing effort substantially, and sometimes dramatically, reduces asynchrony. In consequence, an algorithm for the ventilator adjustment to the individual patient is required. In a similar study, Akoumianaki *et al.* (10) investigated the diaphragmatic muscle contractions triggered by ventilator insufflations as a specific form of patient-ventilator interaction ('entrainment'). In eight ARDS patients, they observed such an entrainment as a reverse triggering varying from 12% to 100% of all breaths during the study period. They conclude that reverse-triggered breath presents a new form of neuromechanical coupling. The clinical consequences have to be determined.

The actual studies, and especially the study by Beitler *et al.* (8), are important contributions to the actual discussion on lung-protective ventilation, which are aimed at detecting and describing dyssynchrony as an occult harm in mechanically ventilated patients. They have some important messages that require more investigations and probably a change in clinical practice:

- A 'troubled' interaction between patient and ventilator is the reality in 'daily practice' MV, and dyssynchrony happens frequently even under the 'surface' of controlled MV;
- Dyssynchrony and breath stacking have the potential to harm the lung, and may counteract lung-protective strategies;
- New technical standards and a scientifically based synopsis with manufacturers are needed (11) to develop an advanced monitoring and early detection of BSD or other forms of disturbed patient-ventilator interactions;
- The increase of sedation or analgesia is not a successful strategy for reducing dyssynchrony;
- An early switch from controlled MV to modern techniques of augmented spontaneous ventilation [proportional assist ventilation (PAV) (12), neurally adjusted ventilator assist (NAVA) (13)] are promising strategies aimed at optimizing the ventilator's response to the specific breath-by-breath demands of the patient;
- Patient-ventilator asynchrony: 'Adapt the ventilator, not the patient' (14).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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