Commentary

**Assisted spontaneous breathing during early acute lung injury**

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**Abstract**

In the early phase of their disease process, patients with acute lung injury are often ventilated with strategies that control the tidal volume or airway pressure, while modes employing spontaneous breathing are applied later to wean the patient from the ventilator. Spontaneous breathing modes may integrate intrinsic feedback mechanisms that should help prevent ventilator-induced lung injury, and should improve synchrony between the ventilator and the patient's demand. Airway pressure release ventilation with spontaneous breathing was shown to decrease cyclic collapse/recruitment of dependent, juxtadiaphragmatic lung areas compared with airway pressure release ventilation without spontaneous breathing. Combined with previous data demonstrating improved cardiorespiratory variables, airway pressure release ventilation with spontaneous breathing may turn out to be a less injurious ventilatory strategy.

Patients with acute lung injury (ALI) or its most severe form, acute respiratory distress syndrome (ARDS), usually require mechanical ventilation. The goals of mechanical ventilation are to decrease the oxygen costs of breathing and to improve gas exchange while minimizing iatrogenic lung injury — so-called ventilator-induced lung injury (VILI). Patients with ALI/ARDS are often ventilated with ventilatory modes and strategies that control the tidal volume or airway pressure in the early phase of the disease process, while modes using assisted spontaneous breathing (SB) are often applied later to facilitate weaning the patient from the ventilator.

The rationale underlying this approach is supported by studies showing that employing controlled mechanical ventilation with low tidal volumes, with limited airway pressures, and with positive end-expiratory pressure (PEEP) attenuates VILI [1] and decreases nonpulmonary organ dysfunction [2,3] and mortality in patients with ALI/ARDS [3].

In a recent survey of clinical practice in 361 intensive care units, Esteban and colleagues found that only about 15% of patients with ARDS were ventilated with a SB mode in the first days [4].

It has been suggested that ventilatory modes in which patients breathe spontaneously early in the course of the ALI process might have advantages such as improved pulmonary ventilation/perfusion (V/Q) matching, increased blood oxygenation, preserved cardiac function, reduced need for excessive sedation, and prevention of ventilation-associated respiratory muscle dysfunction [5-15].

Adaptation of patients to controlled mechanical ventilation often requires deep sedation and occasionally muscle paralysis. Assisted SB is based on the hypothesis that integration rather than abolition of physiological feedback and intrinsic defence mechanisms, such as the Hering–Breuer reflex [16], should help prevent VILI, and should better account for the typically rapid changes in lung mechanics and metabolic demands in ALI/ARDS patients than ‘caregiver’-controlled mechanical ventilation. Little is known to date, however, about the patient’s intrinsic breathing pattern and response to lung collapse, alveolar oedema, and consolidation during ALI/ARDS. Ma and colleagues showed that reflex loops regulating both end-inspiratory and end-expiratory lung volumes are still functional and might help protect the lungs from overdistension and collapse even when lung compliance is decreased [17].

Airway pressure release ventilation (APRV) is a mode of mechanical ventilation introduced by Stock and Downs to...
improve oxygenation during SB [18]. With APRV the pressure in the ventilator circuit is periodically changed between a high level and a lower level, and SB is allowed in any phase of the cycle. The high and low pressure levels, the rate of change between the two levels, the respiratory system compliance, and the airway resistance to flow are the main determinants of the ‘mechanical ventilation’ portion with APRV, while the complementary ‘SB’ portion mainly depends on the patient’s respiratory drive. In contrast to continuous positive airway pressure (CPAP), APRV interrupts the airway pressure briefly to augment spontaneous minute ventilation – thereby increasing alveolar ventilation and CO₂ removal without increasing the work of breathing. SB efforts during APRV are not actively assisted except for those breaths that happen to occur during the change from the lower pressure level to the upper pressure level. Total minute ventilation with APRV is the sum of the mechanical, pressure-controlled ventilation and the complementary SB. APRV without SB is equal to pressure-controlled ventilation.

In a previous issue of Critical Care, Wrigge and colleagues report the effect of APRV with and without SB on lung aeration, on ventilation distribution, and on tidal lung collapse and recruitment assessed by dynamic computed tomography in pigs with oleic-acid-induced ALI [19]. APRV with SB as compared with APRV without SB resulted in increased aeration and ventilation, and in less cyclic collapse/recruitment of dependent, juxtadiaphragmatic lung areas. This study extends previous observations that maintaining SB during mechanical ventilation prevents formation of lung atelectasis [7], and thereby improves the V/Q match in the lungs [9].

Wrigge and colleagues used a uniform, relatively low level of PEEP in all animals, noting that application of higher PEEP levels might have better restored the end-expiratory lung volume and might have reduced cyclic alveolar collapse during APRV without SB. Indeed, application of a preset, uniform PEEP level in subjects with ALI/ARDS does not take into account individual physiologic responses and might therefore lead to alveolar recruitment and putative benefits in some patients, while in other patients recruitment may not occur and there may only be adverse effects [20].

**Assisted SB and synchrony to the patient’s demand**

Assisted SB should ideally be in synchrony and in proportion to the patient’s demand, and should unload respiratory muscles and reduce the patient’s work required to inflate the lungs. The measurement of the patient’s respiratory demand and monitoring the interaction between the ventilator and patient is not straightforward, however. The airway pressure and flow tracings have important limitations for the detection of SB efforts, and although monitoring of oesophageal pressure changes is more reliable it is only rarely used in clinical practice. Detection of the diaphragm electrical activity, which most directly represents the neural output to the respiratory system, potentially offers advantages for monitoring the patient’s respiratory demand but is not yet commercially available [21]. Ventilator parameters for assisted SB such as assistance levels, trigger sensitivity, and criteria to terminate inspiratory gas flow (cycling-off criteria) are chosen mainly based on clinical assessment, on assumptions, and on algorithms.

The work of breathing is shared between the patient and the ventilator during assisted SB. The work of breathing encompasses the force required to overcome the resistance of the airways to airflow as well as the elastic recoil of the lungs and the chest wall. In patients with reduced lung compliance, such as those with ALI/ARDS, inspiration requires considerable respiratory work, especially at low lung volumes [22]. With application of CPAP or PEEP the lung is prevented from collapsing, and inspiration begins from a more favourable point on the pressure–volume curve (i.e. less work is required to expand the lungs). This is also the case during the high pressure level with APRV. Indeed, CPAP titrated individually has been shown to increase lung compliance and to reduce the work of breathing in patients with ALI [23].

Patient–ventilator asynchrony is common, can result in increased inspiratory and expiratory muscle activity [24], and is normally resolved clinically by either adapting ventilator settings, increasing sedation levels, or both [25]. Matching the assistance delivered by the ventilator with the patient’s demand is challenging. None of the currently used SB modes is exempt from patient–ventilator asynchrony, especially when assistance levels are high [26,27]. Increasing sedation levels can result in respiratory muscle unloading but can also result in a monotonous breathing pattern, which may blunt the advantages anticipated from maintained respiratory muscle activity [28]. If the levels of CPAP or PEEP, the settings to trigger and cycle-off the ventilator, and the level of assistance delivered do not meet the patient’s demand, the oxygen cost and the work of breathing may actually increase [29].

Wrigge and colleagues used APRV, a ventilatory mode which entails several interesting concepts. First, APRV overcomes shortcomings related to triggering and cycling-off the ventilator typically inherent to modes of assisted SB, by simply avoiding the inspiratory and expiratory valves in the ventilator circuit [18]. This allows the patient to breathe unhindered. The time-cycled release of airway pressure is not synchronized to the patient’s breathing efforts, however, and may therefore result in cyclic recurrent patient–ventilator asynchrony. Second, the application of CPAP recruits some atelectatic areas, increases the lung volume, and allows SB to occur on a portion of the pressure–volume curve where impedance to airflow is low and only a small transpulmonary pressure change is required to produce the tidal volume. Finally, APRV maintains airway pressures at high levels for a prolonged time. As alveoli are continually recruited along the inspiratory limb of the pressure–volume curve and not just...
below the lower inflection point, as was previously assumed [30], the recruitment of alveoli is likely to be more efficient with APRV than with a shorter application of positive pressure (e.g. as with pressure support ventilation).

**Assisted SB, ventilation/perfusion matching, and cardiac output**

ARDS causes alveolar collapse primarily in dependent lung regions adjacent to the diaphragm, resulting in a venous admixture (V/Q mismatch) and arterial hypoxemia [31]. In a classic article, Froese and Bryan demonstrated that SB in subjects in the supine position results in more marked movement of the posterior diaphragm as compared with the ventral tendon plate [7]. This was associated with increased ventilation of the dependent, usually well-perfused, parts of the lung, whereas during controlled ventilation air was preferentially distributed to the nondependent, less well-perfused, parts of the lungs. Ventilation of a larger share of the lung along with an increase in blood flow to previously minimal or nonperfused areas may help convert shunt units to units with a normal V/Q distribution.

Continuous positive pressure ventilation and PEEP help to improve arterial oxygenation but also affect the intrathoracic to extrathoracic vascular pressure gradients, such that return of blood flow to the right ventricle is impaired and pulmonary vascular impedance is increased (at least with high PEEP levels), resulting in enhanced right ventricular afterload. The combination of both mechanisms is believed to represent the major determinants of the depression of cardiac output during mechanical ventilation [32]. Periodic reduction of intrathoracic pressure combined with compression of intraabdominal vascular beds during SB facilitates venous return to the heart [5] and is associated with decreased pulmonary vascular resistance [10,32]. Increased cardiac output has been found in some [5,6,8-11], but not all [14,15,33], studies evaluating SB in patients with ALI/ARDS. Furthermore, SB in patients with ALI/ARDS was associated with an increase in kidney perfusion, glomerular filtration rate and sodium excretion [8,34], and splanchnic perfusion [35] when compared with controlled mechanical ventilation.

Theoretically, the increase in cardiac output and arterial oxygen content (increased global oxygen delivery) associated with SB during ALI/ARDS may be counterbalanced by an increase in global oxygen demand resulting from the activation of the respiratory muscles during SB efforts. The total oxygen consumption was not measurably altered, however, and the mixed venous oxygen content was higher during SB in a number of studies [10,11,14,36-38] when compared with controlled-mode mechanical ventilation. The global tissue oxygen supply was consequently increased.

**Implication of the present study**

The current study by Wrigge and colleagues suggests another nonhaemodynamic, nongas-exchange-related potential advantage of SB with APRV over controlled ventilation. Wrigge and colleagues demonstrate that APRV with SB led to improved tidal ventilation of dependent juxta-diaphragmatic lung regions, and most importantly led to less cyclic lung collapse. Why might this be important? A number of studies have demonstrated that cyclic lung collapse can lead to increased VILI, manifested by morphologic [39] and biochemical changes such as release of mediators into the lung [1] and into the circulation [40]. This mechanism may explain the development of multiple organ dysfunction syndrome [41].

The study by Wrigge and colleagues was not designed to assess parameters of VILI, so we do not know for sure whether this occurred. Nonetheless, the decreased lung collapse/reopening of the lung suggests that APRV with SB may mitigate VILI and potentially improve outcomes in ALI/ARDS.

Only a few studies have assessed SB in patients with ALI [11,14,15,33,42]. Most of these studies have demonstrated beneficial effects of maintained SB on arterial oxygenation, intrapulmonary V/Q matching, changes in haemodynamics, global oxygen transport, and prevention of excessive sedation. But the use of such surrogate physiological endpoints may not tell us whether a specific mode of ventilation is indeed more appropriate for our patients. For example, in the ARDSNet trial that demonstrated a significant decrease in mortality in patients ventilated with 6 ml/kg compared with 12 ml/kg, patients in the 6 ml/kg arm had worse oxygenation in the first 24 hours compared with the larger tidal volume group.

Given the demonstrated beneficial cardiorespiratory effects of maintaining SB in patients with ALI, and the observed potential benefits in terms of decreased VILI in an animal model, it may be time to consider a controlled trial of a mode such as APRV with SB to improve clinically important outcomes in patients with ALI/ARDS.

**Competing interests**

AS is a consultant for Maquet Medical.

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