Editorial

Airway pressure release ventilation (APRV): do good things come to those who can wait?

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The landmark moment for mechanical ventilation (MV) came with the polio epidemic in the 1950s, leading to the widespread use of MV around the world (1). While controlled MV was favoured over the next three decades, the 1980s witnessed a shift from controlled to augmented spontaneous MV. Such a paradigm change was driven by technical improvements in ventilators in terms of fast-reacting valves, microprocessors, better flow delivery, and better triggering. In the following period, an exciting competition began among new modes of spontaneous ventilation aimed at the improvement of patient-ventilator interaction and the patient's comfort, and the preservation of respiratory pump capacity. Following the emergence of synchronized intermittent mandatory ventilation (SIMV), pressure support ventilation (PSV), proportional assist ventilation (PAV), automatic tube compensation (ATC), and a few other such modes, a special mode was first introduced in 1987 (2). It was characterized as the combination of continuous positive airway pressure (CPAP) with a brief release to ambient pressure short enough to generate auto-positive end-expiratory pressure (PEEP) while the patient was allowed to breathe spontaneously throughout the circle. This was called airway pressure release ventilation (APRV).

The physiological hypothesis was that APRV would ideally combine recruitment of the lung by prolonged CPAP and thus high mean airway pressure, including a short release period (preventing alveolar collapse and allowing partly controlled ventilation) with low tidal ('lung protective') spontaneous breathing, thus preventing diaphragm and muscle pump dystrophy (3). In the 'traditional' modes of MV, intensivists and respiratory therapists were accustomed to setting parameters like respiratory frequency, PEEP, level of pressure support, and tidal volume. In APRV, however, they had to set two pressure levels—'low' (P_{low} corresponds to PEEP) and 'high' (P_{high} corresponds to inspiratory pressure)—and two times—'low' (T_{low} corresponds to inspiratory time) and 'high' (T_{high} corresponds to release time)—accompanied by 'superimposed' spontaneous ventilation. The resulting pattern of such a setting is a combination of total PEEP (P_{low} plus auto-PEEP) with controlled ventilation characterized by frequency (60 s divided by the sum of T_{low} plus T_{high}) and inspiratory pressure (P_{high}). Sounds complicated? Yes, it is—especially for those who feel safe living with 'fixed' minute ventilation by setting a fixed frequency and a fixed tidal volume.

The history and overview of prospective randomized studies on the use of APRV in humans was only partly encouraging: While the physiological concept is attractive and in animals models some improvement in the pulmonary gas exchange (4), systemic blood flow, and organ perfusion was found (5), in none of the 23 reviewed human studies [summarized in (6)] was a worse outcome found using APRV compared to controlled positive pressure ventilation (CPPV). On the other hand, many studies observed significant cardiopulmonary stabilization in the APRV

patients compared to patients using 'traditional' controlled ventilation. However, in a large retrospective case series (7) involving 362 patients ventilated by APRV or CPPV, increased time on the ventilator was observed in the APRV group. All these results were sobering, but from a critical point of view, it was probably not the APRV method *per se* to blame; rather, some under-recognized inherent problems might be responsible for the 'negative' studies. For example, a major problem seemed to be that there was no strict definition of APRV allowing a broad variation in the settings (high and low times and pressures using auto-PEEP or not). In a recent systematic review (6), it was not possible to assess the efficacy of APRV since nearly all the study designs differed in defining a certain pattern of breathing as APRV. For example, Putensen *et al.* (8) chose an 'individualized' APRV setting in 24 patients presenting with acute respiratory distress syndrome (ARDS), while the times (goal: normocapnia) and pressures (goal: low pressure 2 cmH_2O above the inflection pressure on a static pressure/volume curve) were set according to each individual patient's lung mechanics. In contrast, in the study by Maxwell *et al.* (9) involving 63 trauma patients with acute respiratory failure, APRV was set in a predetermined way and remained unchanged throughout the study.

A prospective randomized study from China by Zhou *et al.* (10) brought new insights to the uncertainty regarding 'pros' and 'cons' in the APRV debate. This study focused on 138 patients presenting with ARDS who received MV less than 48 h. The setting for patients in the APRV group included high airway pressure according to the last plateau airway pressure, but did not exceed 30 cmH_2O, while the low airway pressure was set at 5 cmH_2O. The release time (T_{low}) was adjusted to terminate the peak expiratory flow rate to ≥50% resulting in some auto-PEEP, and a frequency of 10–14 cycles/min was targeted. Patients in the control group (low tidal volume [LTV]) were placed in a volume-assisted/controlled mode with a tidal volume of 6 mL/kg predicted body weight (not exceeding 30 cmH_2O) and PEEP guided by the ARDS-Network PEEP/FiO_2 chart. The main results were as follows: The APRV patients had a higher median number of ventilator-free days [median: 19 (range, 8–22) days] compared to the LTV-ventilated patients [median 2 (range, 0–15), P<0.001]. Furthermore, patients in the APRV group had a shorter stay in the ICU (P=0.003), and the ICU mortality rate tended to be lower in the APRV group (19.7%) compared to the LTV group (34.3%, P=0.053). Regarding the respiratory variables 3 days after begin of the study a significant higher PEEP, and higher pressures of the respiratory system (peak, plateau) were noticed in the LTV group, but the driving pressures were not significantly different between the groups. As expected due to higher mean airway pressures, patients in the APRV group demonstrated significantly better PaO_2/FiO_2 ratios three days after enrolment compared to LTV patients (P=0.001), along with improved hemodynamic variables (mean arterial and diastolic pressures). The rate of ventilation-associated complications (pneumothorax, barotrauma) did not differ between the groups.

Is the study by Zhou *et al.* the beginning of a renaissance for APRV as the 'best' ventilation mode in (early) acute lung injury/ARDS, combining lung protection with assisted spontaneous breathing? No, it is too early to rejoice about having found the philosopher's stone. First, the study by Zhou *et al.* (10) has some limitations: It is not blinded, which is an inherent limitation for nearly all intervention studies in critical care. Furthermore, patients in the LTV group had a significantly higher rate of comorbidities (P=0.029) compared to the APRV group. Additionally, it is accepted that the outcome parameter 'length of ICU stay' is no longer a good parameter, since the transfer of a patient from the ICU to a normal ward or rehabilitation is guided by many variables which are not associated with the patient's condition. Second, we have learnt from many other studies that the application of just one strategy in a heterogeneous patient group characterized by a syndrome like ARDS (which is not a clearly defined disease!) often does not lead to significant results automatically. Meanwhile, the call for individual and personalized medicine has reached the area of care for the critically ill (11).

Third, an important issue was not touched upon in this study, but is of high relevance: the importance of patient-ventilator interaction and the level of dys-synchrony in such a mixed mode of controlled and spontaneous ventilation (12). In past years, the influence of augmented spontaneous ventilation modes on synchrony and the work of breathing (WOB) was examined (13). Although augmented spontaneous ventilation modes like bi-phasic positive airway pressure or APRV should be theoretically advantageous in terms of a patient's WOB or patient–ventilator synchrony, such a benefit was not demonstrated in patients with acute lung injury (12). Furthermore, in the present era of lung protective ventilation, we lack sufficient data on whether spontaneous breathing in the early phase of acute lung failure may counteract lung protection by increased dys-synchrony and high spontaneous tidal volumes (14). In the study by Zhou *et al.* (10), such a physiological conflict

was 'circumnavigated' by relatively deep sedation of the patients (mean Richmond Agitation-Sedation Scale score on Day 3: –2.9). In other words, based on the present study by Zhou *et al.*, we cannot conclude that APRV prevent patient-ventilator dys-synchrony and/or negative effects on lung protection induced by spontaneous ventilation *per se* in patients who are relatively awake. To answer such a complex question, further studies are needed that include the parameters of (dys-)synchrony (assessments of esophageal pressure) and lung protection (markers of inflammation).

In summary, the merit of the work by Zhou *et al.* (10) is that it contributes to a more optimistic re-evaluation of APRV. The combination of controlled ventilation with patient-guided spontaneous ventilation should form the focus of further investigations, since the physiological advantages of APRV (adequate mechanical support to offload the respiratory muscles) are still attractive. On the other hand, whether such a mode fulfils all the criteria for lung protective ventilation has to be determined in future. At present, we cannot claim that the early application of airway pressure release ventilation in ARDS is a 'therapy for all!' (15,16).

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Footnote

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

References

1. Slutsky AS. History of Mechanical Ventilation. From Vesalius to Ventilator-induced Lung Injury. Am J Respir Crit Care Med 2015;191:1106-15.
2. Stock MC, Downs JB, Frolicher DA. Airway pressure release ventilation. Crit Care Med 1987;15:462-6.
3. Daoud EG, Farag HL, Chatburn RL. Airway pressure release ventilation: what do we know? Respir Care 2012;57:282-92.
4. Wrigge H, Zinserling J, Neumann P, et al. Spontaneous breathing improves lung aeration in oleic acid-induced lung injury. Anesthesiology 2003;99:376-84.
5. Hering R, Viehöfer A, Zinserling J, et al. Effects of spontaneous breathing during airway pressure release ventilation on intestinal blood flow in experimental lung injury. Anesthesiology 2003;99:1137-44.
6. Jain SV, Kollisch-Singule M, Sadowitz B, et al. The 30-year evolution of airway pressure release ventilation (APRV). Intensive Care Med Exp 2016;4:11.
7. Maung AA, Schuster KM, Kaplan LJ, et al. Compared to conventional ventilation, airway pressure release ventilation may increase ventilator days in trauma patients. J Trauma Acute Care Surg 2012;73:507-10.
8. Putensen C, Mutz NJ, Putensen-Himmer G, et al. Spontaneous breathing during ventilatory support improves ventilation-perfusion distributions in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 1999;159:1241-8.
9. Maxwell RA, Green JM, Waldrop J, et al. A randomized prospective trial of airway pressure release ventilation and low tidal volume ventilation in adult trauma patients with acute respiratory failure. J Trauma 2010;69:501-10; discussion 511.
10. Zhou Y, Jin X, Lv Y, et al. Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in acute respiratory distress syndrome. Intensive Care Med 2017;43:1648-59.
11. Nieman GF, Satalin J, Andrews P, et al. Personalizing mechanical ventilation according to physiologic parameters to stabilize alveoli and minimize ventilator induced lung injury (VILI). Intensive Care Med Exp 2017;5:8.
12. Kallet RH. Patient-ventilator interaction during acute lung injury, and the role of spontaneous breathing: part 2: airway pressure release ventilation. Respir Care 2011;56:190-203; discussion 203-6.
13. Calzia E, Lindner KH, Witt S, et al. Pressure-time product and work of breathing during biphasic continuous positive airway pressure and assisted spontaneous breathing. Am J Respir Crit Care Med 1994;150:904-10.
14. Mauri T, Cambiaghi B, Spinelli E, et al. Spontaneous breathing: a double-edged sword to handle with care. Ann Transl Med 2017;5:292.
15. Esnault P, Prunet B, Nguyen C, et al. Early application of airway pressure release ventilation in acute respiratory distress syndrome: a therapy for all? Intensive Care Med 2018;44:135-6.
16. Myers TR, MacIntyre NR. Respiratory controversies in the critical care setting. Does airway pressure release ventilation offer important new advantages in mechanical ventilator support? Respir Care 2007;52:452-8; discussion 458-60.

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