Editorial

Improve survival from prolonged mechanical ventilation: beginning with first step

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Although conventional invasive mechanical ventilation is a life-saving procedure for critically ill patients, it is the most important risk factor for ventilator-associated events (VAEs) (1-3). Patients with VAEs often need prolonged mechanical ventilation (PMV), which leads to increased family and financial burden (1) and worse prognosis (2). However, long-term outcomes associated with PMV are not fully understood (3). A recent meta-analysis reporting long-term survival of critically ill patients treated with PMV further highlights the worse prognosis posed by the patients (3). Pooled mortality associated with PMV at hospital discharge, 1 year, and beyond 1 year was 29% (95% CI: 26-32), 62% (95% CI: 57-67), and 66% (95% CI: 61-70), respectively. Moreover, only 19% [16-24] were discharged to home and only 50% [47-53] were successfully liberated from mechanical ventilation (MV). These results alarm the physicians that PMV increases not intensive care unit (ICU) and hospital mortality, but long-term mortality. Considering the worse short-term and long-term outcomes of PMV, timely and effective weaning from PMV is an important priority in primary care for critically ill patients. However, difficult or prolonged weaning is common and effective management weaning remains unclear. If physicians and intensivists focus on the problems, a first step to improve the outcomes of patients with PMV is reducing the incidence of PMV.

Predictors of difficult or prolonged weaning

Peñuelas screened the weaning patients, and clarified simple, difficult and prolonged weaning (2). About 69% patients can be extubated at the first weaning attempt (simple weaning), while the remaining 31% need more than one spontaneous breathing trial (SBT) (difficult plus prolonged weaning) (4). Difficult weaning includes patients who required up to 7 days being extubated from the first attempt of withdrawal from mechanical ventilation. Prolonged weaning refers to failure at least three weaning attempts or required >7 days of weaning after the first SBT. Predictors for difficult or prolonged weaning include high simplified acute physiology score II score, duration of MV before simple weaning, chronic pulmonary disease, pneumonia, high PEEP before simple weaning (2). However, airway and lung dysfunction, brain dysfunction, cardiac dysfunction, diaphragm/respiratory muscle function and endocrine and metabolic dysfunction also could induced difficult or prolonged weaning.

Reducing incidence of difficult or prolonged weaning

Focusing on the primary disease is the first line treatment for reducing the incidence of prolonged weaning. Besides the primary diseases control, there are some the do's and don'ts needing attention.

Screen the reasons of prolonged weaning

After intubating the patients, the first purpose of the treatment is weaning from the ventilator. Heunks classified the reasons of a difficult to wean patients: airway or lung dysfunction, brain dysfunction, cardiac dysfunction, diaphragm dysfunction, and endocrine dysfunction (5). Critically ill patients in ICU may have continuing organ

failures leading to protracted periods of organ support (6). Therefore, it is a key step of weaning that primary disease and the complications are controlled.

Optimal mechanical ventilation settings

Improper settings could induce lung injury, especially for acute respiratory distress syndrome (ARDS) patients. Although hospital mortality of ARDS patients is approximately 40%, 1-year mortality decreases to 14% and 3-year mortality is only 15% (7,8). Even the patients treated with extracorporeal membrane oxygenation (ECMO), the 261-day survival is 86% (9), and the survivors had minor lung disabilities with diminished diffusion capacities across the blood-gas barrier (10). If acute lung injury is controlled, it may not influence long-term outcomes of these patients. Therefore, it is essential to establish optimal ventilation strategy to protect lung and improve hospital mortality. The ventilation strategy include: low tidal volume (6 mL/kg predict body weight), optimal PEEP level, plateau pressure <30 cm H_2O, and prone position in ARDS patients with PO_2/FiO_2 <150 mmHg (11). Moreover, Amato in the retrospective study showed that mortality of ARDS patients was associated with driving pressure (12), but the threshold value of the pressure needs to be further clarified.

Early transfer to non-invasive ventilation (NIV)

NIV has been used in weaning protocol for chronic obstructive pulmonary disease (COPD) patients. It could reduce intubation rates and improve ICU mortality (13-15). NIV also could be used in weaning of acute respiratory failure patients, and NIV after early extubation could decrease invasive-ventilation-days and reintubation rates within 48 hours (16,17). However, further studies are needed to explain the characteristics of the patients and the protocol.

Avoiding ICU-acquired weakness

ICU-acquired weakness is an important reason which directly leads to prolonged weaning. The pathophysiological mechanisms of ICU-acquired weakness are multifactorial. Both of critical illness polyneuropathy and critical illness myopathy could induce ICU-acquired weakness. Moreover, sepsis, persistent systemic inflammation, multiorgan system failure, long duration of mechanical ventilation, immobility, hyperglycemia, and the use of glucocorticoids or neuromuscular blocking agents are important risk factors.

Ventilator induced diaphragm dysfunction (VIDD) is the important clinical manifestation of ICU-acquired weakness, and it could induce prolonged weaning. There are many risks contributing to VIDD, e.g., sepsis, mechanical ventilation, corticosteroids using and inflammatory factors (18). Some treatments should be administrated for the patients with mechanical ventilation. Firstly, system inflammatory response syndrome (SIRS) and sepsis should be controlled. Secondly, measures how much benefits the patients can get from corticosteroids, and some antioxidant supplementation (alpha-tocopherol and ascorbic acid) may be benefit for VIDD (19). Thirdly, keeping spontaneous breath and using assisted ventilation mode could improve diaphragm movement, neurally adjusted ventilatory assist ventilation should be the better mode for the difficult and prolonged patients weaning (20,21). Fourthly, sufficient nutrition could help the patients recovery from VIDD (22).

Early progressive mobilization

The strategy for whole-body rehabilitation could improve mechanical patients' functional outcomes and ventilator-free days, decrease incidence of delirium, length of ICU and hospital days (23). Many studies have proved early mobilization is safe and effect for the critically ill patients (24,25), but when and how to start early mobilization protocol is still debated. However, an expert consensus and recommendations could be used for safety criteria. Mobilizing patients in ICU may be considered according to a traffic-light system of low risk of an adverse event (green), potential risk of an adverse event is outweighed by the benefit of early mobilization (yellow) and significant potential risk of an adverse event requiring consultation with senior ICU staff (red) (26), and awakening and breathing coordination, delirium monitoring/management, early exercise/mobility (ABCDE) bundle could help to the treatment of implementation (25).

Light sedation and delirium controlled

Light sedation is associated with improved clinical outcomes (e.g., shorter duration of mechanical ventilation and length of ICU stay). Therefore, the guidelines for the management of pain, agitation, and delirium recommend maintaining light levels of sedation in adult ICU patients (27). Delirium is associated with prolonged length of ICU and hospital stay, increased mortality, and long-term cognitive impairment in ICU patients (28). Early mobilization of the

patients and avoiding benzodiazepine usage could prevent delirium (27).

Improve endocrine and metabolic dysfunctions

Difficult weaning induced by endocrine and metabolic dysfunctions is usually ignored. Adrenal insufficiency, hypothyroidism, and electrolyte disturbances (e.g., very low plasma levels of phosphate and magnesium) are associated with difficult and prolonged weaning (5). These diseases should be taken into consideration when treating difficult weaning patients.

In conclusion, physicians and intensivists should pay more attention to critically ill patients receiving PMV. How to improve long-term outcomes of these patients needs the further study. If we could reduce the risks of PMV at the first step, these patients will start on the journey towards better outcomes.

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