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WHAT'S NEW IN INTENSIVE CARE

Update on acute respiratory failure

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Acute respiratory failure remains a leading diagnosis early after admission to an Intensive Care Unit (ICU) producing an enormous healthcare burden. Despite the health care improvements along the last decades, its associated high mortality has only slightly dropped, remaining up to around 30% in most severe cases [1]. A huge amount of information is generated every year on respiratory failure and its management in the intensive care environment, but the limited progress in mortality seems more related to improvements in general care for critically ill patients [1]. As a general rule, research on severe acute respiratory failure is evolving towards two main headings: phenotyping patients attempting to generate more homogeneous clinical groups with predictable responses to applied therapies and a better balance between protecting the lungs and the rest of the organs.

Phenotyping

Ever since acute respiratory distress syndrome (ARDS) was defined, first phenotyping related to severity and escalating therapy was based on oxygenation, according to PaO_2/FiO_2 severity thresholds; however, ventilator-induced lung injury (VILI) determinants, mainly the respiratory mechanical properties and ventilator settings, are mostly unrelated to oxygenation impairment. Thus, it should be reconsidered escalating respiratory support based on oxygenation impairment [2].

Awake prone has become a widely used intervention for patients with acute respiratory failure under spontaneous breathing conditions. However, the heterogeneous response, in part secondary to differences in tolerance, of those patients hinders a wider use. The ROX index increase within the first 6 h of the prone trial coupled with baseline characteristics helps clinicians to predict the response and mortality [3].

Phenotyping can also improve the response to neuromuscular blocking agents and corticoids. The former based on baseline life expectancy determined by age and comorbidities with greater benefit in those younger and without fatal comorbidities [4], and the latter in terms of characterization of inflammatory phenotype using clinical surrogate data. Thus, those with inflammatory ARDS should be prioritized to receive corticoids, and titrated according to monitoring transition to hypoinflammatory state [5].

On the other hand, personalizing treatment does not always reach a significant improvement in clinical studies. A recent trial failed to obtain a meaningful clinical benefit when a strategy of individually adjusting the highest positive end expiratory pressure (PEEP) in targeting driving pressure in patients at risk for postoperatory respiratory failure was used [6]. It should be always kept in mind that personalizing ventilator settings is time consuming at the bed side, sometimes turning unfeasible adequate monitoring. Although pragmatic approaches can counterbalance this increased intricacy, sometimes go against personalization, as titrating the highest PEEP level up to a target driving pressure ≤ 13 cm H_2O can also have participated in this negative result.

Protecting the lungs but not only the lungs

Early switch to spontaneous invasive mechanical ventilation is gaining progressive evidence to improved outcomes in patients with acute respiratory failure. Interestingly, partial switch using a pressure-driven controlled-spontaneous breathing keep the benefit, not only for lung function in terms of reduced need to escalating treatment for hypoxemia, but also extra-lung organ function, mainly the brain as the need for sedatives is reduced [7]. In addition, ARDS patients under spontaneous breathing, PEEP titration can be optimized in a patient-by-patient basis with advanced respiratory monitoring

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using electrical impedance tomography and transpulmonary pressure monitoring. Once again, coupling treatment according to lungs and brain requirements in terms of controlling respiratory drive seems to be the reason for the respiratory improvement, without worsening neurological outcome [8]. This reinforces the idea that personalization and pragmatism cannot be always coupled.

Extracorporeal membrane oxygenation (ECMO) is the ultimate line of defense of the severely injured lung and heart. While research on long-term lung rest and ultraprotective ventilation consecuences is pending, new insights to titrate ventilation during ECMO therapy suggest that short-term ultraprotective ventilation compared to lung rest in patients undergoing scheduled cardiac surgery does not reduce postoperative infections [9].

Optimal fluid management in patients with ARDS is challenging, but Joseph et al. confirmed the reliability of dynamic indices to predict fluid responsiveness in patients with ARDS although with distinct thresholds. Hypovolemia is associated with mortality in these patients, while fluid responsiveness alone is not [10].

Protecting the entire process

First-line noninvasive respiratory support for de novo respiratory failure is a controversial topic for which we still do not have a definitive answer. While currently high flow oxygen is recommended as first line therapy, aspects like optimized setting noninvasive ventilation by increasing PEEP level leaves room for improving the response to second-line treatments [11]. In addition, patients with worse response to high flow like those immunocompromised, detecting early the risk for failing and lack of response is of highest relevance [12]. Accelerate weaning is a cornerstone of this process and advances on the spontaneous breathing trial (SBT) and models predicting extubation failure deserve mention. Deciding the type of SBT trying to emulate the work of breathing after extubation has not been confirmed in clinical studies, but there may be room for T-tube trials in some types of patients, such as those with brain injury or after abdominal surgery [13].

Current clinical models used to decide post-extubation noninvasive respiratory support have good sensitivity and negative predictive value, assuring that no high-risk patients are left behind to receive preventive therapy after extubation, but their low specificity and positive predictive value must be interpreted in the context of over-prevention and the effectiveness of the preventive therapies under which these analyses were performed. The complexity to define risk for failing extubation is coupled to the growth armory to optimize postextubation noninvasive support in a patient-by-patient basis [14].

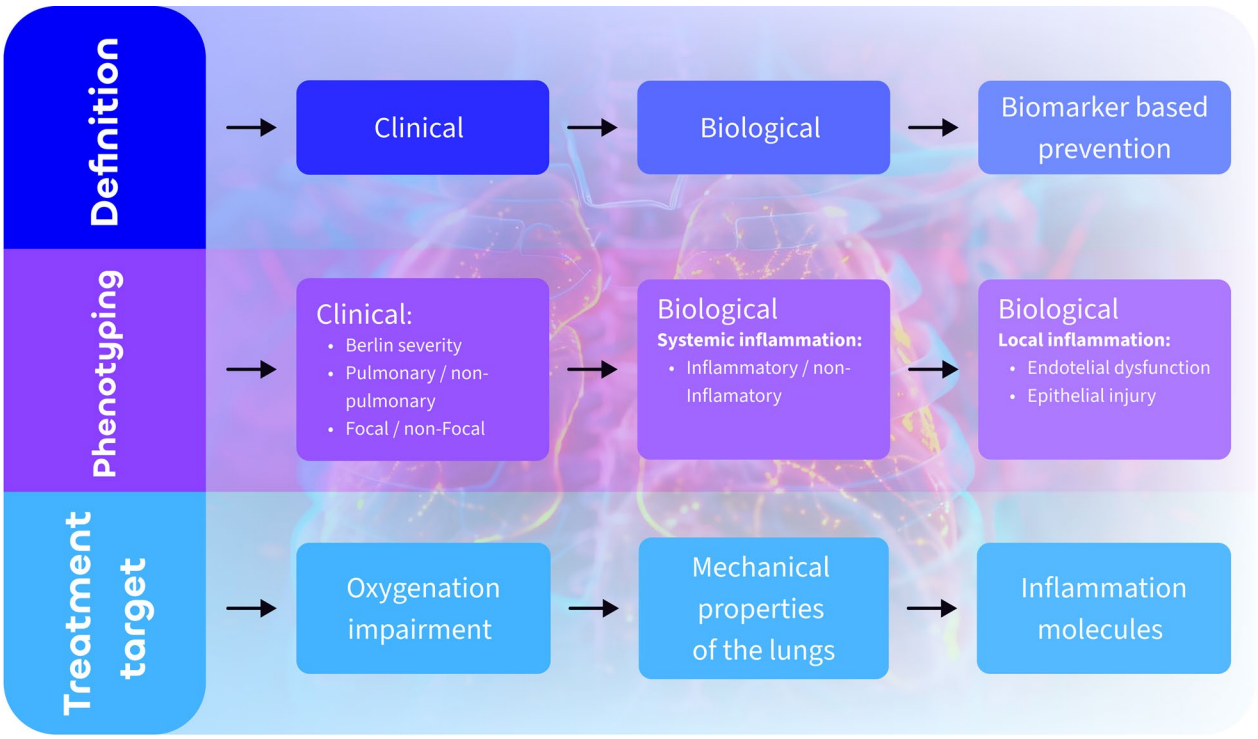

Fig. 1 Direction for improving outcomes in acute respiratory failure

Future directions: what can we expect from translational research?

New studies open the possibility of biomarker-guided ventilation. López-Martinez and coworkers [15] have pooled a large number of studies on gene and micro-RNA expression during ventilator-induced lung injury, to find transcriptomic signatures linked to lung overdistension. They found a collection of microRNAs that can be measured in tissue, brochoalveolar lavage fluid, and serum. Moreover, the authors made all the data available via a webapp, allowing any reader to explore the whole dataset. Evolving to personalized ventilator settings and targeting therapies also for inflammatory targets represents a hope for prognosis improvement in acute respiratory failure patients (Fig. 1).

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Data availability statement
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Declarations

Conflicts of interest
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