Highlights from the Respiratory Failure and Mechanical Ventilation Conference 2024

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Shareable abstract (@ERSpublications)
Practical key points concerning acute and chronic respiratory failure in adults from the Respiratory Failure and Mechanical Ventilation Conference 2024 https://bit.ly/4gxqKnd

Cite this article as: Bianquis C, De Leo G, Morana G, *et al*. Highlights from the Respiratory Failure and Mechanical Ventilation Conference 2024. *Breathe* 2024; 20: 240105 [DOI: 10.1183/20734735.0105-2024].

Received: 24 May 2024
Accepted: 19 Aug 2024

Abstract

The Respiratory Intensive Care Assembly of the European Respiratory Society gathered in Berlin to organise the third Respiratory Failure and Mechanical Ventilation Conference in February 2024. The conference covered key points of acute and chronic respiratory failure in adults. During the 3-day conference ventilatory strategies, patient selection, diagnostic approaches, treatment and health-related quality of life topics were addressed by a panel of international experts. In this article, lectures delivered during the event have been summarised by early career members of the Assembly and take-home messages highlighted.

Introduction

In this summary of the third Respiratory Failure and Mechanical Ventilation Conference, held in Berlin in February 2024, the early career members of the European Respiratory Society (ERS) Respiratory Intensive Care Assembly provide an overview of highlights from the conference programme. This report includes sessions in acute and chronic respiratory failure which were delivered by international experts in the field. It covers symposia on the state-of-the-art in veno-venous extracorporeal membrane oxygenation (ECMO), noninvasive ventilation (NIV) and high-flow therapy (HFT), but also addresses artificial intelligence (AI) in mechanical ventilation, prevention of weaning difficulties, diagnostic challenges in acute respiratory failure (ARF) with definition and phenotypes of acute respiratory distress syndrome (ARDS), and finally sets out the goals of chronic home ventilation and of amyotrophic lateral sclerosis (ALS) treatment.

State of the art: veno-venous ECMO

Holger Müller-Redetzky (Berlin, Germany) described the eligibility criteria for veno-venous ECMO (vvECMO) according to the EOLIA study (table 1) [1, 2] and the evidence for vvECMO in ARDS [3]. The EOLIA study showed a better prognosis when vvECMO was initiated early (<7 days) [1]. In addition, practitioners can use the several other parameters, such as age, immunosuppression, *etc.*, to predict

TABLE 1 Enrolment criteria for the EOLIA trial

Patients were eligible for enrolment if they fulfilled the American–European Consensus Conference definition for ARDS, were endotracheally intubated and receiving ventilation for <7 days, and had one of the following disease-severity criteria despite ventilator optimisation[#]:

1) P_{aO_2}:F_{IO_2} ratio <50 mmHg for 3 h despite optimisation of mechanical ventilation and despite potential use of various usual adjunctive therapies (inhaled nitric oxide, recruitment manoeuvres, prone position, HFO ventilation, almitrine infusion); OR
2) P_{aO_2}:F_{IO_2} ratio <80 mmHg for >6 h, plus the other criteria noted in point 1; OR
3) Arterial blood pH <7.25 with P_{aCO_2} ⩾60 mmHg for >6 h (with respiratory rate increased to 35 breaths per min) resulting from mechanical ventilation settings adjusted to keep P_{plat} ⩽32 cmH_2O.

ARDS: acute respiratory distress syndrome; P_{aO_2}: arterial oxygen tension; F_{IO_2}: inspiratory oxygen fraction; HFO: high-frequency oscillation; P_{aCO_2}: arterial carbon dioxide tension; P_{plat}: plateau pressure. [#]: F_{IO_2} ⩾80%, tidal volume 6 mL per kg predicted body weight and positive end-expiratory pressure >10 cmH_2O. Information from [1].

survival [4]. Moreover, better survival was seen when patients were evaluated at an experienced ARDS/ECMO centre (as demonstrated in the CESAR TRIAL) [5]. A further improvement in survival is expected when patients are referred to high-volume ECMO centres (>30 patients per year) [6].

Christian Karagiannidis (Cologne, Germany) discussed the implications of the control of respiratory drive during vvECMO [7], which is indicated for patients admitted for ARDS, whether ventilated or not, or intubated or not. The respiratory drive and effort can be reduced by vvECMO by increasing the removal of blood carbon dioxide. In ARDS patients, the reduction of arterial carbon dioxide tension (P_{aCO_2}) permits maintenance of the tidal volume in a potentially safe range [8, 9]. Furthermore, in COPD patients with a severe acute exacerbation, the control of the respiratory drive reduces dynamic hyperinflation [10] and eventually avoids intubation [11]. Recently, extracorporeal carbon dioxide elimination ($ECCO_2R$) has been shown to facilitate extubation in severe COPD exacerbation [12].

Domenico L. Grieco (Rome, Italy) highlighted the effects of the ventilator settings on the outcome of patients on vvECMO [13]. Conventional protective ventilation [14] or more extreme strategies, *i.e.* near-apnoeic ventilation [15], are necessary to decrease the risk of ventilator-induced lung injury and patient self-inflicted lung injury (P-SILI). Currently, no correlation has been found between positive end-expiratory pressure (PEEP) level and patient outcomes [16], hence PEEP should be set individually [17, 18]. The role of vvECMO during weaning from invasive mechanical ventilation was discussed [9]. In this scenario, ECMO may be used to reduce the respiratory effort in patients at higher risk for P-SILI during the spontaneous breathing trial [18, 19]. Finally, prone positioning did not show any benefit in reducing weaning time from vvECMO, but no adverse effects of the procedure have been reported either [20].

Take-home messages

- vvECMO may reduce mortality in severe ARDS when initiated early (<7 days) and when patients are transferred to an experienced high-volume centre (>30 cases per year).
- The control of respiratory effort in patients on vvECMO may reduce the risk of lung damage and may facilitate extubation during the spontaneous breathing trial.
- A thorough management of mechanical ventilation in patients on vvECMO is essential for patient outcomes.

Artificial intelligence in mechanical ventilation

Björn Weiss (Berlin, Germany) presented Berlin's experience with telemedicine in intensive care units (ICU) and home mechanical ventilation, addressing the challenges experienced in German intensive care, including staff shortages and changing care structures. The implementation of a telemedicine network aimed to standardise treatment and enhance quality through evidence-based protocols. Using telemedicine as a catalyst, the ERIC project [21] demonstrated tangible improvements in adherence to quality indicators, particularly in areas such as sedation, analgesia and infection management. However, its impact on mortality and ventilation duration was less pronounced [22]. Nevertheless, the initiative laid the groundwork for standardised care pathways and intersectoral management strategies for patients in the ICU and transitioning out of the ICU. Telemedicine showed promise in bridging care gaps and enhancing outcomes, especially during the COVID-19 pandemic. Future initiatives aim to expand telemedicine internationally for intersectoral care in chronic critical illness cases [23].

Andreas Schuppert (Aachen, Germany), a data scientist from Germany, delved into the fundamental principles of AI in healthcare, emphasising the distinction between weak, strong and generative AI phenotypes. Weak AI, which is prevalent in medical applications, encompasses supervised, unsupervised, reinforcement and transfer learning. A. Schuppert elucidated the underlying concept of AI, highlighting its ability to learn common features from diverse data sets. He discussed the potential and limitations of AI, including the curse of dimensionality and the need for extensive data for accurate learning. A. Schuppert examined the current state of the art of AI in ICU care, highlighting its potential for early diagnosis in mild ARDS [24], prognosis, and therapy optimisation [25]. He discussed the challenges faced in implementing AI, including data quality and explainability. Strategies for optimising therapy through digital twin simulations and cross-disease transfer learning were also discussed. Finally, he outlined the path forward to realise the full potential of AI, emphasising the need for improved data availability, implementation strategies, and integration of medical knowledge with AI technologies.

Pedro David Wendel Garcia (Zurich, Switzerland) discussed the increasing prominence of AI in emergency medicine and ICUs. He highlighted a surge in AI-related publications in recent years and defined AI as software capable of tasks previously believed to require human intelligence. He provided a comprehensive overview of the diverse AI models used in emergency and critical care medicine. He highlighted key models such as neural networks, support vector machines, and decision trees, delineating their respective applications in predicting outcomes, scoring systems, image analysis, and clinical documentation assistance. P.D. Wendel Garcia showcased the promise of AI in revolutionising clinical practice, citing examples of improved patient outcomes through early sepsis detection [26] and optimised treatment protocols [27]. The role of AI in image analysis [28], disease phenotyping, and waveform analysis [29] was discussed, emphasising its potential to enhance diagnostic accuracy, workflow efficiency and treatment decision making [30]. P.D. Wendel Garcia highlighted the importance of robustness, reproducibility [30], and ethical considerations in AI implementation, stressing the need for homogenised big data landscapes, robust reporting guidelines and actionable AI solutions tailored to clinical settings.

Take-home messages

- As telemedicine continues to evolve, its role in transforming healthcare delivery and improving patient outcomes remains a central focus of research and innovation efforts.
- AI represents a new technology with unseen flexibility in complex scenarios. By complementing expert knowledge, it offers high potential for diagnosis decision support and optimisation in clinical settings.
- To bridge the gap between AI model development and real-world clinical outcomes it is fundamental to have homogenised big data landscapes, robust reporting guidelines, and actionable AI solutions tailored to clinical settings.

Difficult weaning – is it preventable?

Leo Heunks (Nijmegen, the Netherlands) posed the question of whether the type of spontaneous breathing trial will affect the outcomes. It seems that a shorter, less demanding spontaneous breathing trial strategy should be prioritised among patients with a high risk of extubation failure [31], although in the largest cohort study more than 30% of patients who were successfully weaned never had a spontaneous breathing trial declared [32].

Many questions arise along the way from controlled to assisted ventilation, to extubation. The WEAN-SAFE study attempted to answer these questions, showing that while 65% of patients were weaned within 90 days, many needed prolonged weaning [32]. The success rate was influenced by sedation levels at the time of weaning eligibility and delayed spontaneous breathing trials [33]. Weaning challenges the respiratory reserve. An “ABC of weaning failure” could help to evaluate airway, brain, cardiac, diaphragm and endocrine disorders as causes [34].

Lara Pisani (Bologna, Italy) reported that diaphragm dysfunction is seen in up to 64% of ICU patients and correlates with prolonged weaning. Both decreased and increased diaphragm thickening are associated with prolonged ICU stay [35]. Therefore, the concept of diaphragm protective ventilation has been raised. Expiratory muscle recruitment indicates high respiratory load and muscle weakness and is associated with worse outcomes.

Ultrasound can be used to monitor respiratory muscle function along with pressure measurements and electromyography. Diaphragm and intercostal muscle thickening predicts spontaneous breathing failure. Their over-recruitment leads to dynamic airway collapse, a rise in end-expiratory lung volume, small airway and alveolar injury, and finally, atelectasis and tidal recruitment leading to ARDS. By contrast,

their weakness leads to a reduction in ventilation and coughing capacity, and a drop in the secretion clearance (figure 1).

$ECCO_2R$ reduces respiratory drive in COPD and increases weaning readiness; however, in the study presented the sequence of weaning trials was not randomised, so exclusion of a time effect to explain the improvement in respiratory parameters during the second trial cannot be excluded. The results encourage future investigations on the use $ECCO_2R$ to facilitate the weaning process [36]. Preventive approaches like diaphragm neurostimulation-assisted ventilation and expiratory muscle stimulation are under investigation.

Nicholas Hart (London, UK) returned to the findings of WEAN-SAFE to explore if technology could accelerate weaning. Variations of weaning practices contribute to weaning failure. Automated systems may reduce weaning duration [37, 38], but not mortality [39]. Neurally adjusted ventilatory assist showed clinical benefits and shorter weaning without affecting mortality [40].

Take home messages

- Weaning is a crucial moment and a complex task, whether it is simple, difficult or prolonged.
- Weaning protocols, eligibility recognition, and sedation have a role in reducing the duration.
- Respiratory muscles play a role in weaning outcomes, routine monitoring can be useful.
- Future evaluation is needed for up-and-coming methods, for example, $ECCO_2R$, neurostimulation, neurally adjusted ventilatory assist, and automated weaning modes.

ARDS: definition and phenotypes

Christian Karagiannidis (Cologne, Germany) presented a comprehensive assessment of all ARDS definitions, including their relative changes over time [2, 41]. He emphasised the need for having a global definition of ARDS, especially given its mortality and prevalence in low- and middle-income countries where achieving diagnostic criteria may be challenging due to a lack of resources [42–44]. He stressed the interest of ERS Assembly 2 to be involved in the future and recommended an international societies-guided definition.

Alexandre Demoule (Paris, France) discussed the role of lung ultrasound (LUS) for diagnosing ARDS [45]. He presented an explanation of the pathophysiology of LUS [46–48] and showed the ability to score non-aerated lung regions at the bedside. Short-term training on LUS is sufficient to build expertise [49],

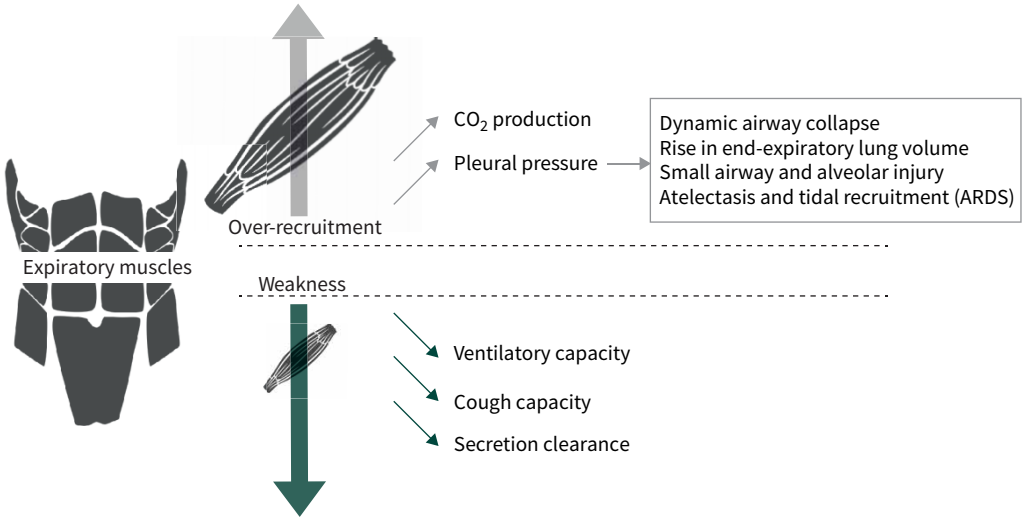

FIGURE 1 Figure illustrating the pathophysiological effects resulting from over-recruitment and conversely caused by weakness of the expiratory muscles. Over-recruitment leads to an increase in carbon dioxide production and pleural pressure, with the overall consequences of dynamic airway collapse, a rise in end-expiratory lung volume, small airway and alveolar injury, and finally, atelectasis and tidal recruitment leading to acute respiratory distress syndrome (ARDS). Weakness of the expiratory muscles leads to a reduction in ventilation and coughing capacity, and a drop in the clearance of secretions.

and this can increase the likelihood of diagnosing ARDS, especially in resource-limited settings [50]. LUS can effectively predict ARDS [51] and can be used to set PEEP during mechanical ventilation [52].

Marry Smit (Utrecht, the Netherlands) defined the ARDS sub-phenotypes based on imaging, physiological and biological characteristics. Sub-phenotypes respond to different treatments and have different prognoses [1, 53–63]. The hyper-inflammatory/hypo-inflammatory sub-phenotype is the most investigated [64], and novel machine learning models based on biomarkers and clinical data are showing promising results for identification of this sub-phenotype [65, 66]. This sub-phenotype may also be extended to mechanically ventilated critically ill patients without ARDS [67].

Lieuwe D.J. Bos (Amsterdam, the Netherlands) discussed sub-phenotype driven randomised controlled trials (RCTs) and the role of precision medicine in developing innovative strategies for prognostic and predictive enrichment to optimise patient selection [68, 69]. L.D.J. Bos proposed three domains for ARDS phenotyping: aetiology, physiology and biology [70]. He concluded his presentation by showing some ongoing trials and their potential role in identifying subgroups with similar biological characteristics, especially at the bedside, that may respond similarly to specific interventions [71].

Several clinical trials are underway on the phenotyping of ARDS (ClinicalTrials.gov registration numbers: NCT04157946, NCT06083363, NCT06001645).

Take-home messages

- A global, medical societies-guided definition of ARDS is needed.
- LUS can help to diagnose and manage ARDS (*e.g.* to set PEEP, to decide if prone positioning is needed, to phenotype and personalise ventilation strategy, and to predict weaning failure).
- Identification of phenotypes and sub-phenotypes of ARDS is mandatory to provide a tailored treatment for patients and additional funding is needed for large sub-phenotype based RCTs.

Goals of chronic home ventilation

Physiological outcomes, significant patient outcomes and expected social outcomes of chronic ventilation were discussed, as well the considerations to achieve these goals in children.

Wolfram Windisch (Cologne, Germany) helped us to understand the importance of targeting physiological outcomes, arterial carbon dioxide reduction, and how to ventilate some categories of patients using high-intensity NIV [72, 73]. In patients with COPD and interstitial lung disease high-intensity NIV could relieve the workload on respiratory muscles, in addition to the effects of low-intensity NIV (figure 2) [74]. Successful high-intensity NIV would be achieved by adequate inspiratory pressure and by a reduction of arterial carbon dioxide level, subsequently leading to improved dyspnoea, lung function, quality of life and cardiac function [75, 76].

Peter J. Wijkstra (Groningen, the Netherlands) showed data about the relationship between NIV application and various improvements in patient-related outcomes, particularly sleep and quality of life [77–79]. He highlighted the vital components to achieve patient-relevant outcomes: patient type [80], adequate level and duration of support [74], timing to start NIV [80] and preferably home initiation [81, 82].

Rebecca D'Cruz (London, UK) invited us to delve deeper into meaningful outcomes at the societal level. While access to home ventilation helped patients with physiological needs, it came with high costs imposed on society [83]. The productivity of society should be considered, which might be commenced by addressing the method to support quality of life and promote productive societal engagement of patients [84].

Hui Leng Tan (London, UK) shared information about caring for domiciliary ventilated children, who require regular monitoring to ensure the appropriate settings and minimise side-effects (*e.g.* midface hypoplasia). There are an increasing number of children receiving NIV [85] due to improved technology and perceived benefits [86]. To achieve the quality-of-life goals, physicians need to address different issues found in children with neuromuscular disease [86, 87], neurodisability [88] and congenital hypoventilation syndrome [89].

Take-home messages

- Applying chronic home ventilation requires an understanding of the key physiological derangements correlated with the patient-important outcomes, effective mode of ventilation, timing to initiate and specific needs of each patient.

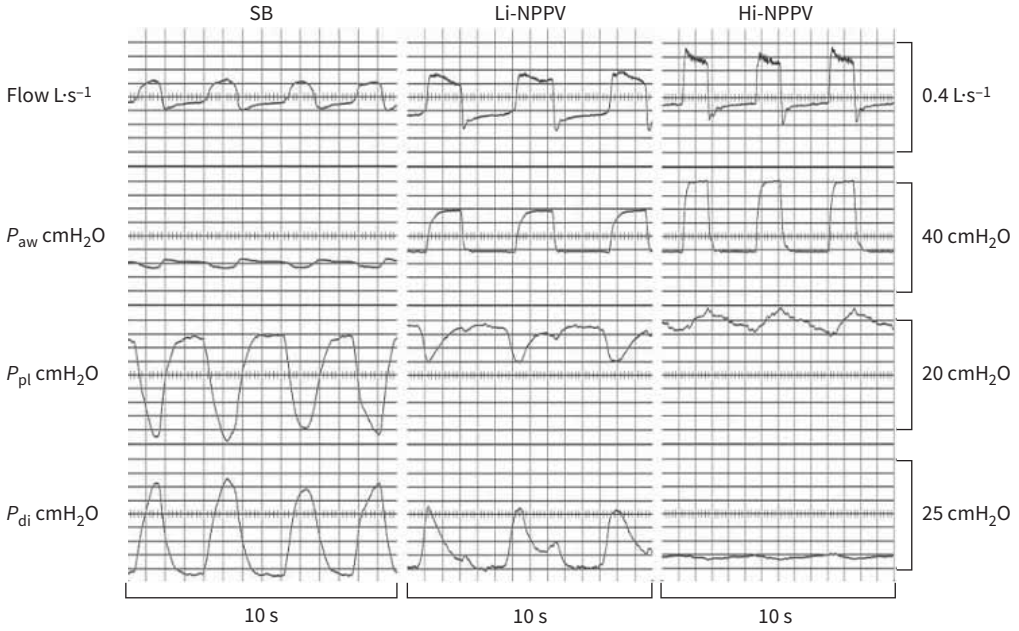

FIGURE 2 Respiratory mechanical parameters during spontaneous breathing (SB), low-intensity (Li-) noninvasive positive pressure ventilation (NPPV) and high-intensity (Hi-) NPPV. Transdiaphragmatic pressure (P_{di}) was lowest during Hi-NPPV. P_{aw}: airway pressure; P_{pl}: pleural pressure. Reproduced from [74] with permission.

- The goal of home ventilation could be the correction of physiological abnormalities, enhancing quality of life. and ideally, promoting social functioning of an individual.

ALS – timing, goals and effectiveness

Peter J. Wijkstra (Groningen, the Netherlands) pointed out that NIV improves survival and quality of life in patients with ALS [90]; however, the beneficial effects depend on the patient's phenotype and on the timing of introduction [91]. NIV is usually indicated in patients with P_{aCO_2} >45 mmHg or forced vital capacity (FVC) <50% or orthopnoea, but a RCT showed that starting NIV in patients with seated FVC <75% might reduce respiratory events [92]. French experts recommend starting NIV as soon as FVC is <80% in the sitting position in association with another abnormality on pulmonary function testing [93]. However, in specially selected patients such as those with frontotemporal dementia a survival benefit of NIV has not been shown and therefore, the indication for NIV in these patients should be assessed on an individual basis [94].

In general, the decision to start NIV must also consider the different means of long-term monitoring at home [95]. NIV settings should take into account laryngeal response in patients with airway clearance to prevent avoidable NIV failures [96].

Berry Everts (Groningen, the Netherlands), an ALS patient, shared his thoughts on ventilatory support. After having 3 months of fatigue and sleepiness, which impacted him a lot, starting NIV improved his quality of life significantly. He has been taught many care skills by the nurses. He is now NIV-dependent for 23–24 h per day and has the freedom to change the settings a certain amount. He uses the mouthpiece ventilation during social dinners. The patient has had a discussion about tracheostomy and has declined it, however, this might change in the future.

João Carlos Winck (Vila Nova de Gaia, Portugal) outlined predictors of the need for tracheostomy in ALS. These include full-time dependency on NIV with peripheral oxygen saturation <95% and a progressive decline in peak cough flow with a mechanical insufflation–exufflation device [97, 98]. Tracheostomy prolonged survival for ALS patients [99]. There are big differences in prevalence of tracheostomy among countries worldwide (<1–50%) [100–105]. This is probably because of the additional care to provide for the more complex needs induced and the few but potentially severe complications, such as decannulation, obstruction and haemorrhage.

Formal patient education about tracheostomy can change a lot [106]. Today, some technologies can assist tracheostomised patients in different aspects of life such as socialising, entertainment and accessing the internet [107].

Take-home messages

- NIV and tracheostomy ventilation prolongs survival and can improve quality of life when addressed to the right patient at the right time.
- Good nurse–patient interactions and education are very important for ALS patients' decision making.

Diagnostic challenges in acute respiratory failure

Martin Witzenrath (Berlin, Germany) opened the session with a presentation on the management of severe community-acquired pneumonia (CAP). Recent studies have highlighted how the integration of omics data could significantly improve CAP stratification risk [108]. Diagnostic methodologies must be adapted according to whether patients are immunodeficient or immunocompetent [109]. Adjunctive therapy with hydrocortisone has been demonstrated to reduce the risk of death in patients with severe CAP [110, 111]. Cardiovascular events appeared to be more frequent during pneumonia due to increased overall systemic inflammation and neutrophil activity [112, 113].

Miquel Ferrer Monreal (Barcelona, Spain) gave an overview of the recognition and treatment of ventilator-associated pneumonia (VAP). The introduction of molecular techniques, such as RT-PCR, has increased the diagnostic yield and accelerated the use of appropriate antimicrobials [114]. Therapy must incorporate the high prevalence of Gram-negative bacteria, such as Enterobacteriaceae and *Pseudomonas aeruginosa*, which are the most frequent pathogens in VAP [115]. Newly available antibiotics have improved the management of VAP from drug-resistant microorganisms, with greater efficacy in more severe patients [116].

The topic of viral reactivations in non-resolving lung injury was discussed by Lieuwe D.J. Bos (Amsterdam, the Netherlands). Herpesviridae viruses are characterised by lytic replication with host cell breakdown, resulting in increased tissue damage [117, 118]. In preliminary data, herpes simplex virus (HSV) reactivation is common in mechanically ventilated patients with COVID-19 [119]. The HSV viral load is associated with mortality; antiviral treatment has been shown to lower the risk of death. The immunological signature of HSV reactivation is characterised by high levels of interleukin (IL)-6, IL-1β and tumour necrosis factor-α, which persists even after antiviral treatment.

Fungal infections in non-resolving lung injury were presented by Joost Wauters (Leuven, Belgium). Pulmonary aspergillosis associated with COVID-19 and influenza occurs in 5–20% of cases, mainly in immunocompromised patients [120]. The use of corticosteroids is an independent risk factor for the development of pulmonary aspergillosis [121]. The pathological role of *Candida* colonisation is currently poorly understood, as it may have immunomodulatory activity, supporting neutrophil activation [122]. Bronchoalveolar lavage with positive culture or galactomannan is essential for the diagnosis of invasive pulmonary aspergillosis [123].

Take-home messages

- Cardiovascular events are more frequent during pneumonia.
- New antibiotics for drug-resistant microorganisms have improved the outcomes of patients with severe VAP.
- HSV reactivation is associated with increased mortality in mechanically ventilated COVID-19 patients.
- COVID-19- and influenza-associated pulmonary aspergillosis is frequent in immunocompromised patients.

Precision medicine in noninvasive respiratory support strategies in acute and chronic respiratory failure

Domenico Grieco (Rome, Italy) discussed the use of NIV and HFT in ARF [2] and the uncertainty associated with this matter. Noninvasive strategies aim to support the patient, but the risk of P-SILI due to dysregulation of respiratory effort must be considered [124, 125]. Different strategies have different effects on the patient's respiratory effort, especially NIV [126, 127]. HFT is suggested as the first-line intervention for hypoxaemic patients [128]. Noninvasive tools to measure respiratory effort must be evaluated, such as carbon dioxide tension, nasal occlusion pressure [129] or surface electromyogram.

In the area of chronic respiratory failure (CRF), Lara Pisani (Bologna, Italy) analysed the scarce evidence on the use of NIV in stable COPD patients with CRF [130]. After an acute exacerbation there may be a spontaneously reversible hypercapnia [131, 132], so NIV should only be considered after an evaluation 2–4 weeks after the event. The use of HFT can be considered in hypoxaemic COPD patients [133], and in recent studies it also appears to be useful in hypercapnic COPD patients [134, 135], since this treatment reduces the incidence of moderate-to-severe exacerbations. A trial to assess the impact of HFT solely regarding the incidence of severe exacerbations is currently underway (ClinicalTrials.gov registration number: NCT05196698). The use of asymmetrical cannula has a role in optimising HFT use [136].

Alessandro Amaddeo (Trieste, Italy) discussed the use of noninvasive therapies in children [137], which have been used in the intensive care setting. HFT is one of the most valuable therapies to use in viral bronchiolitis [137, 138], but continuous positive airway pressure (CPAP) can also have a role [139].

Begüm Ergan (Izmir, Turkey) reviewed the process of weaning from noninvasive support in patients with ARF. The appropriate timing of weaning is crucial to prevent recurrence or complications, and this should be based on gas exchange, other physiological values, and patient improvement [140, 141]. Predictive tools, such as the ROX index and LUS, can be used to aid decision making [142, 143]. There are several weaning strategies, including reduction in time, immediate discontinuation, pressure reduction in NIV, and flow or oxygen reduction in HFT [144–146].

Take-home messages

- HFT should be suggested as the first-line treatment in hypoxaemic respiratory failure, but NIV can be considered even though evidence is lacking.
- NIV is the recommended therapy in COPD patients with hypercapnic CRF, but the evidence on the use of HFT is increasing.
- HFT can be used in children with ARF. When there is no response, CPAP is a reasonable rescue therapy.
- NIV and HFT weaning timing and strategies are yet to be defined due to the heterogeneity of patients. Complete withdrawal of support may not be possible in some patients.

Conflict of interest: C. Bianquis reports grants from ASTEN santé and support for attending meetings from Vitalaire. G. De Leo, G. Morana, M. Duarte-Silva and S. Nolasco have nothing to disclose. R. Vilde reports support for attending meetings from Chiesi and has a leadership role with Latvian Junior doctors' association as a Board member. A. Tripipitsiriwat and P. Viegas have nothing to disclose. M. Purenkovs reports leadership roles with the Latvian Society of Sleep Medicine (Board member), Latvian Society of Innovative Pneumonology and Respiratory Medicine (board member), and Latvian Society of Tuberculosis and Lung Diseases doctors (board member). M. Duiverman reports grants from Fisher & Paykel (High-TeC trial), Vivisol BV (High-TeC trial and Noctivent trial), RESMED Ltd (RECAPTURE trial), Löwenstein BV (Noctivent trial), and Secure BV (Noctivent trial), payment or honoraria for lectures from Vivisol BV, Chiesi, Breas, and AstraZeneca, and a leadership role with ERS as the chair of the NIV group of Assembly 2. C. Karagiannidis and C. Fisser have nothing to disclose.

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