

Early View

Invited review

ERS International Congress, Virtual 2021: Highlights from the Respiratory Intensive Care Assembly Early Career Members

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ERS International Congress, Virtual 2021: Highlights from the Respiratory Intensive Care Assembly Early Career Members

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Abstract

Early Career Members of Assembly 2 (Respiratory Intensive Care) attended the European Respiratory Society Annual Congress through a virtual platform in 2021. Sessions of interest to our Assembly members included Symposia on the implications of acute respiratory distress syndrome (ARDS) phenotyping on diagnosis and treatment, safe applications of non-invasive ventilation (NIV) in hypoxaemic respiratory failure and new developments in mechanical ventilation and weaning, and a Guidelines session on applying high-flow therapy (HFT) in acute respiratory failure. These sessions are summarised in this article.

Introduction

Assembly 2 of the European Respiratory Society encompasses the broad fields of Respiratory Critical Care. Our assembly is divided into two groups, those of acute critical care and of non-invasive support. Currently, our assembly is headed by Professor Leo Heunks, Professor João Winck has the role of secretary, and Dr Maxime Patout is our Early Career Representative. The acute critical care sub-group is chaired by Professor Christian Karagiannidis, with Professor Ignacio Martin-Loeches as secretary. The non-invasive support group is chaired by Dr Mareike Duiverman, and Dr Claudia Crimi is secretary. At the time of publication, we have 1553 Assembly two members, 36% of whom are early career members. A recent highlight of Assembly 2 was our organisation of the inaugural Respiratory Failure and Mechanical Ventilation conference, which was held in Berlin in March 2020. This was a great success, with attendees arriving from around the world to enjoy engaging and educational seminars delivered by expert panels, workshops and lectures within the streams of adult acute respiratory failure, chronic respiratory failure and paediatric respiratory failure (1). Early career members had the opportunity to present cases and posters and to chair sessions. We look forward to the second meeting, which will be held in Berlin between 9th and 11th June 2022. In this review, we present highlights from the European Respiratory Society Annual Congress 2021 of interest to Assembly 2 members and those interested in critical care and mechanical ventilation. The sessions we have reported on include the symposia on acute respiratory distress syndrome phenotypes, non-invasive ventilation in hypoxic respiratory failure and new developments in mechanical ventilation and weaning, and the guidelines session on high-flow nasal cannula in adults with acute respiratory failure.

Symposium – Acute respiratory distress syndrome phenotypes: implications for diagnosis and treatment

Acute respiratory disease syndrome (ARDS) pathophysiology was presented by Nuala Meyer. In the 1970s, ARDS pathophysiology was driven by oxygen toxicity. Since then, ventilator management and supportive care have changed. Epithelial cell death is characteristic but endothelial damage is more subtle (2). However, COVID-lungs autopsy studies showed endothelial damage, microthrombi, and endothelial disruption. Classic cells driving ARDS are predominantly neutrophils and macrophages (3). Neutrophil-derived chlorolipids, neutrophil extracellular traps, are excellent biomarkers for

ARDS (4). Moreover, new cell death mechanisms and pathways may represent novel therapeutic targets in ARDS (5).

Jean-Michel Constantin focused on personalised ventilator settings and implications of lung morphology in ARDS. He reported that the mortality was lower in focal ARDS group than in the non-focal groups despite similar $\text{PaO}_2:\text{FiO}_2$, with different responses to lung recruitment (6). In the non-focal group, the lungs can be ventilated homogeneously with higher positive end expiratory pressure (PEEP), whereas higher pressure can cause overinflation in normal areas in focal group. Therefore, the LIVE study was designed by Constantin and colleagues (7). In the intervention arm of this study, the focal group was ventilated with low PEEP and high tidal volume (8ml/kg) and the non-focal group with low tidal volume and high PEEP. 90-day mortality was similar between groups. However, mortality was higher in those who have been misclassified. In conclusion, dynamic parameters like ultrasound, electric impedance tomography and CT-scan can help choosing the correct ventilator settings.

Charlotte Summers presented biological sub-phenotyping of ARDS. Previously, two sub-phenotypes were identified by retrospectively analysing the ARMA and the ALVEOLI trials (8). The hyperinflammatory group were observed to have higher mortality, while response to higher PEEP and conservative fluid therapy was better (9). Data from the UK Critical Care Genomics, the Northern Ireland Clinical Trials Unit and the MOSAIC Influenza Consortium were integrated to develop disease subtypes. Three types of influenza-associated ARDS were identified as adaptive, endothelial leak and neutrophil-driven (Figure 1). Survival was poorer in the neutrophil-driven subtype.

Figure 1: Neutrophils are identifiable by their multi-lobulated nuclei, and are indicated by blue arrows in this Giemsa stained blood film. Neutrophil-driven hyperinflammatory acute respiratory distress syndrome is associated with higher mortality.

Brijesh Patel talked on individual approaches to resolve lung injury. Pneumonia, lower $\text{PaO}_2:\text{FiO}_2$, higher pressures, higher tidal volume and higher non-respiratory sequential organ failure assessment (SOFA) score were risk factors for persisting ARDS (10). Patel and colleagues used machine learning to report that patients who did not resolve hypoxemia within the first week had higher intensive care unit (ICU) mortality (11). To understand resolution phenotypes, multimodal approaches should be developed combining physiology, radiology, and bioinformatics.

Take home messages:

- ♦ ARDS may be phenotyped using imaging and inflammatory markers
- ♦ A range of imaging modalities may be used, including ultrasound, EIT and CCT
- ♦ Hyperinflammatory ARDS has a poorer prognosis
- ♦ Phenotyping is important to guide the ventilatory strategy, and may impact upon clinical outcomes.

Symposium – NIV in hypoxic respiratory failure: stay safe and know your limits

Luigi Camparota opened the session conceptualizing the assessment of severity of respiratory failure as triangle: gas exchange, radiology and biomarkers and respiratory effort, all connected with a fourth dimension corresponding to the disease evolution in time. The gas exchange reflects two separate phenomena: the alveolar integrity and the functional abnormalities such as dysregulated pulmonary perfusion. The COVID-19 pandemic was used throughout the presentation as model for the different assessment methods, both invasive and non-invasive. Dr Camparota reflected on a commonly used tool, the arterial pressure of oxygen: fraction of inspired oxygen ratio ($\text{PaO}_2/\text{FiO}_2$), and its limitation being dependent of the FiO_2 , making it difficult to assess its evolution in case of change in the denominator. In a recent study, the ROX index (ratio of oxygen saturation as measured by pulse oximetry/ FiO_2 to respiratory rate) has greater predictive validity than NEWS2 for deterioration in COVID-19 (12).

Stefano Nava reported pros and cons of non-invasive respiratory support (NRS) during the COVID-19 pandemic, since NRS was used outside the intensive care setting, where no previous recommendations existed. On one side, studies showed that high-flow therapy (HFT), continuous positive airway pressure (CPAP) and NIV had similar adjusted mortality rate. Helmet and CPAP had a significantly reduced intubation rate compared to HFT (13). Professor Nava challenged the audience with a provocative question: Did we kill HFT? The answer is probably not. HFT must be used in specific situations for its already known indications. On the other side, NRS depends on the severity of hypoxemia. $\text{PaO}_2:\text{FiO}_2$ is dependent of work of breathing (WOB) therefore it does not predict alone lung recruitment and mechanics. Patient effort is important and can contribute to ventilator induced lung injury. Last consideration is staff contamination due to aerosol generation by NRS (Figure 2).

Figure 2 Non-invasive ventilation and high-flow therapy is associated with aerosol generation, therefore appropriate precautions must be taken by healthcare workers to reduce the risk of nosocomial transmission. A range of face masks are

available for use in the healthcare environment, and should be selected based on the type and level of exposure to aerosol generating procedures. The mask shown in the image is an example of a filtering facepiece 3 (FFP3). This type of mask provides a high level of particle filtering with little leak, and is commonly donned in the critical care setting. Surgical face masks are made of non-woven fabric, worn loosely over the nose and mouth. They provide a lower level of protection from airborne disease and should therefore be used in environments where no aerosol generating procedures are performed.

Marieke Duiverman reflected on the role of NRS on refractory breathlessness. A limitation within this area is that most studies include small patient numbers and short-term end-points. A 2015 systematic review concluded that opioids improved breathlessness in patients with severe chronic obstructive pulmonary disease (COPD) (14), although the benefit was lower than the later described minimal clinically important difference (15). Another systematic review demonstrated a slight benefit of NIV in relieving dyspnoea in COPD stable patients (16), but whether it is clinically relevant remains uncertain. In the acute setting, it is essential to define goals life support versus symptom relief, and the side effects patients (and physicians) tolerate depend on these goals. A randomized crossover study showed that HFT was superior to conventional oxygen therapy in reducing the severity of dyspnoea in the first hour of treatment in patients with do-not-intubate status and hypoxemic respiratory failure (17).

In her presentation, Maria Vega illustrated the physiological background in NRS based on a recent review (18), showing lower intubation rate and mortality with NRS compared to standard oxygenation in hypoxaemic respiratory failure. Patient self-inflicted lung injury (P-SILI) and ventilator-induced lung injury (VILI) are influenced by dynamic transpulmonary pressure ($PL = P_{aw} + P_{pl}$) which in turn depends on patient effort (P_{pl}). NIV decreases WOB and therefore personalised pressure titration reduces risk of lung injury. Effect of applied pressure support is determined by oesophageal swing (Figure 3). Strategy of respiratory support should consider patient inspiratory effort to avoid increase dynamic stress.

Figure 3 Oesophageal pressure swing may be used as an indicator of work of breathing. In the above image, the top trace (green) is the oesophageal pressure, the bottom trace is the patient's air flow measured at the mouth.

Take home messages:

- ♦ The $\text{PaO}_2\text{:FiO}_2$ and the ROX index may be used to classify severity of hypoxic respiratory failure
- ♦ Aerosol generation and use of appropriate personal protective equipment must be considered when implementing non-invasive respiratory support (NRS)
- ♦ There are limited data on the use of NRS in breathlessness management, and the burdens of treatment must be weighed up against physiological benefits
- ♦ Patient effort must be considered when selecting an appropriate ventilatory strategy

Symposium – New developments in mechanical ventilation and ventilator weaning

Patient's perspective: Olivia Fulton, a former ICU asthma patient and a volunteer for a charity for post-intensive care patients and their family, discussed her experience in the ICU. She highlighted that patience, communication, and awareness about the patients' ability to hear or feel are the key parameters that ICU personnel need to embrace in order to make the patients' stay in the ICU less traumatic.

Epidemiology and geographical variation in ventilator weaning: John Laffey highlighted that prolonged invasive mechanical ventilation and extubation failure are associated with multiple complications and higher mortality (19). Several types of Spontaneous Breathing Trial (SBT) have been described, but a T-piece trial seems to better reflect work of breathing after extubation compared to pressure support ventilation (PSV) (20). In terms of the epidemiology of weaning, J. Laffey summarized some preliminary results of the WEAN SAFE Study (Worldwide Assessment of Separation of pAtients From ventilatory assistance), which addresses key issues regarding weaning from mechanical ventilation (ClinicalTrials.gov ID NCT03255109). We eagerly await the publication of the full results. The study by Burns et al found significant differences between participating countries regarding the methods and personnel involved in weaning, highlighting the worldwide variation in practices (21).

Personalized mechanical ventilation and weaning in patients with COPD: Lise Piquilloud emphasized that the goal of MV in COPD patients is to reduce hyperinflation. Regarding controlled ventilation, the usual approach is controlled hypoventilation with permissive hypercapnia. During assisted ventilation, the presence of intrinsic positive end-expiratory pressure (PEEPi) leads to

increased work of breathing and asynchronies which may be mitigated by carefully titrating PEEP. Neurally adjusted ventilatory assist (NAVA) ventilates the patient based on the electrical activity of the diaphragm and reduces asynchrony compared with PSV (22, 23). Moreover, NAVA has been associated with reduced duration of MV compared with PSV in patients at risk for prolonged mechanical ventilation (24). L. Piquilloud stressed the importance of daily screening for weaning readiness and early extubation. In COPD patients at risk for extubation failure we must consider the early use of NIV or HFT. When high PEEP_i persists despite appropriate ventilation, we may use extracorporeal carbon dioxide removal (ECCO₂R), which allows us to further decrease minute ventilation with beneficial effects on hyperinflation and mitigation of the deleterious consequences of hypercapnia and acidosis (25). Moreover, ECCO₂R may be used to facilitate weaning, since it may improve work of breathing (26). Nevertheless, more studies are needed to prove its efficacy and safety before it can be used as a general treatment strategy in routine clinical practice.

Lung and diaphragm protective ventilation: Katerina Vaporidi discussed lung injury and protective mechanical ventilation strategies that include optimization of tidal volume (VT) and PEEP, prone positioning and allowing diaphragmatic contraction with early spontaneous breathing. The measurement of transpulmonary end-expiratory pressure by an oesophageal catheter and electrical impedance tomography may aid in PEEP titration. Global tidal lung stress may be monitored by measuring airway driving pressure. However, regional lung stress can be more accurately estimated by the transpulmonary driving pressure. High tidal stress may be mitigated by improving lung homogeneity, avoiding high VT and decreasing ventilatory demands (27, 28). Passive ventilation as well as assisted ventilation can induce diaphragm disuse atrophy. Protective ventilation involves avoiding prolonged diaphragmatic rest, over- or under-assistance and dysynchrony. Titration of inspiratory effort can be achieved with measurement of the pressure time product of oesophageal pressure (PTP_{oes}), while simpler bedside methods include measurement of P_{0.1} and oesophageal pressure swing. Modulating the respiratory drive can help in manipulating the patient's effort (27-29).

The impact of machine learning on mechanical ventilation in critically ill patients: Lucas Fleuren started his lecture by emphasizing the need for processing information. This need may be met by machine learning which includes supervised, unsupervised and reinforcement learning (30). L. Fleuren focused on supervised learning which enables the prediction of outcome based on the input data. Machine learning is increasingly reported in the intensive care literature. Nonetheless, the vast

majority of studies involve model prototyping and development, while there is a paucity of data regarding their implementation into clinical practice (31). An application of the use of machine learning is described in the study by Fleuren *et al.* (32). They used the Dutch Data Warehouse (DDW), a multi-centre electronic health record database, to determine the most important predictors for extubation failure. L. Fleuren argues that the next step is the determination of the appropriate parameters that will be used in research so that machine learning can assist clinicians in their everyday practice.

Take home messages:

- ♦ Measures should be taken to minimise the short- and long-term psychological impact of a critical care admission for patients, including clear and appropriate methods of communication
- ♦ Readiness to wean should be assessed daily and may involve spontaneous breathing trials, t-piece ventilation and pressure support ventilation, and results from the WEAN SAFE study are awaited
- ♦ In COPD, hyperinflation may be managed with controlled hypoventilation and permissive hypercapnia, and patients may benefit from post-extubation non-invasive ventilation or high-flow therapy.
- ♦ Protective ventilation strategies should be implemented to avoid lung injury and diaphragm atrophy
- ♦ Advances in machine learning may be a valuable adjunct to clinical evaluation to support critical care management

Guidelines session – High flow nasal cannula in adults with acute respiratory failure

There is a strong physiological rationale for the use of high flow therapy (HFT) in hypoxemic respiratory failure, and justification for its application in hypercapnic respiratory failure (33-37) (Figure 4).

Figure 4 Schematic of high-flow therapy (HFT) setup. HFT may deliver flow rates up to 60-100 L/min and facilitate delivery of a stable FiO₂ up to 100%. Heating, humidification and a high flow rate confers a range of physiological benefits. Reproduced under CC BY-NC 4.0 license from D'Cruz RF et al., High-flow therapy: physiological effects and clinical applications, *Breathe* 2020 16: 200224.

Recent meta-analyses have reported its superiority compared to conventional oxygen therapy (COT) in terms of endotracheal intubation and mortality reduction (18, 38-40). Moreover, when compared with other therapies such as helmet NIV, the risk of patient self-inflicted lung injury is lower with HFT (41). Considering the beneficial effects of both HFT and NIV, it is plausible that the combination of therapies might achieve better outcomes than a single treatment approach (42-44). Regarding the applicability of HFT for COVID-19 patients, it has been widely used throughout the pandemic, with observational data indicating favourable results (45, 46), which also apply in the prone position (47), and might be more useful than other non-invasive strategies in the early stages of the disease (48). Given that it is possible that HFT failure could delay intubation and increase mortality (49), it is mandatory for these patients to be monitored in specifically designed physical spaces such as Respiratory Intermediate Care Units or the Intensive Care Unit, where healthcare personnel safety can also be optimised. A practical tool is the ROX index, which has been validated in patients with ARDS on HFT, with an index greater than 4.88 after initiation consistently associated with a lower risk for intubation (50). This index may be useful for COVID-19 patients as well (51).

After a thorough systematic review and consensus of experts, the summary of Guideline recommendations is:

1. For acute hypoxemic respiratory failure, it is suggested to use high-flow therapy over conventional oxygen therapy and non-invasive ventilation. As well, guideline authors suggest using HFT over COT during breaks from NIV.
2. In a post-operative scenario, either COT or HFT may be used in patients with lower risk of respiratory complications, and either HFT or NIV should be applied for patients at higher risk of respiratory complications.
3. Following extubation from invasive mechanical ventilation in non-surgical patients, authors recommend use of HFT in preference to COT in patients at low or moderate risk of extubation failure, and the use of NIV over HFT in those at high risk of failure, unless there are relative or absolute contraindications to NIV.

4. For hypercapnic respiratory failure, the Guideline suggests a trial of NIV prior to use of HFT in patients with COPD.

Take home messages:

- ♦ High-flow therapy (HFT) is an effective treatment in acute hypoxaemic respiratory failure
- ♦ HFT is associated with better clinical outcomes when used post-extubation compared to conventional oxygen in those at low risk of post-extubation respiratory failure
- ♦ HFT is a safe intervention that is tolerated well by patients and is associated with a lower incidence of interface-related skin damage and lung injury compared to non-invasive ventilation
- ♦ Non-invasive ventilation is first-line therapy in COPD patients with acute hypercapnic respiratory failure after a period of medical management
- ♦ HFT may be used effectively in COVID pneumonitis, however patients should be monitored closely for deterioration and invasive mechanical ventilation initiated early if necessary

(2827 words)

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Figure 1

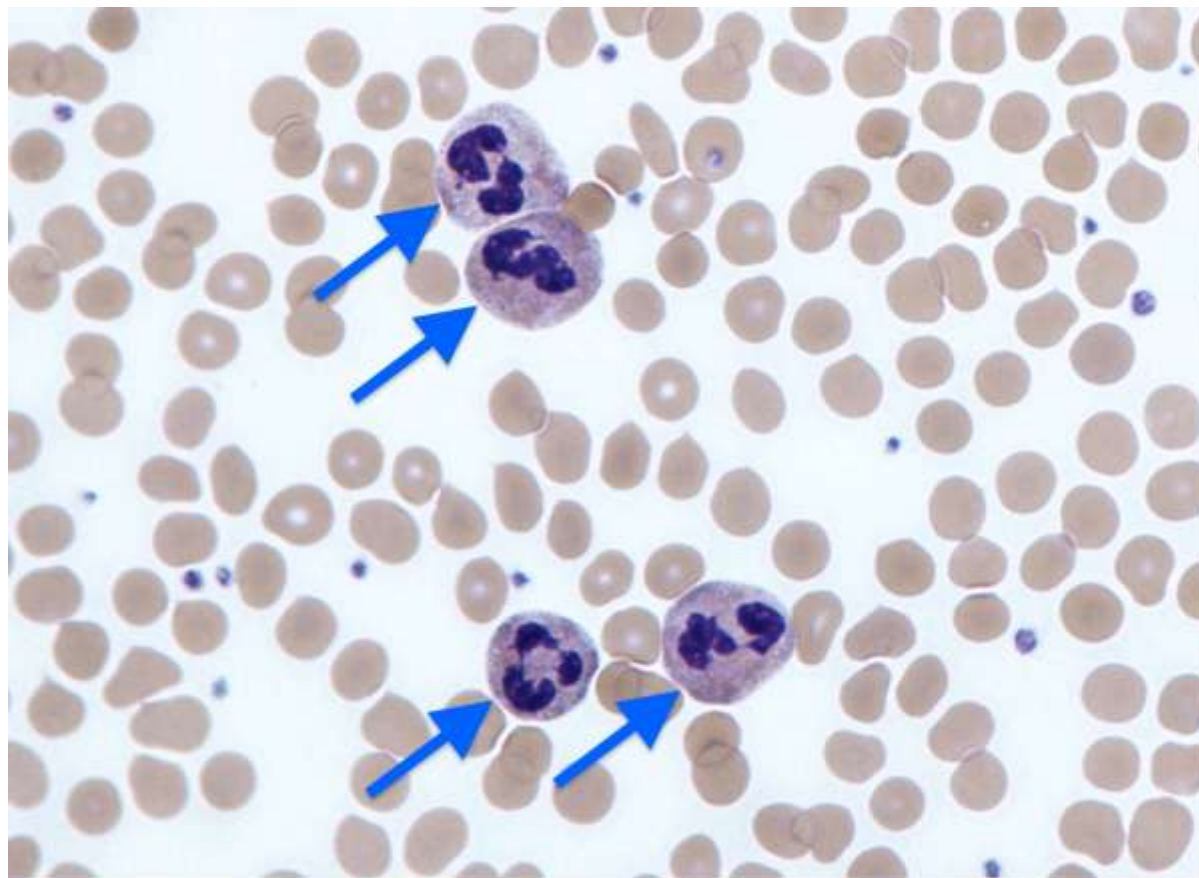


Figure 2



Figure 3

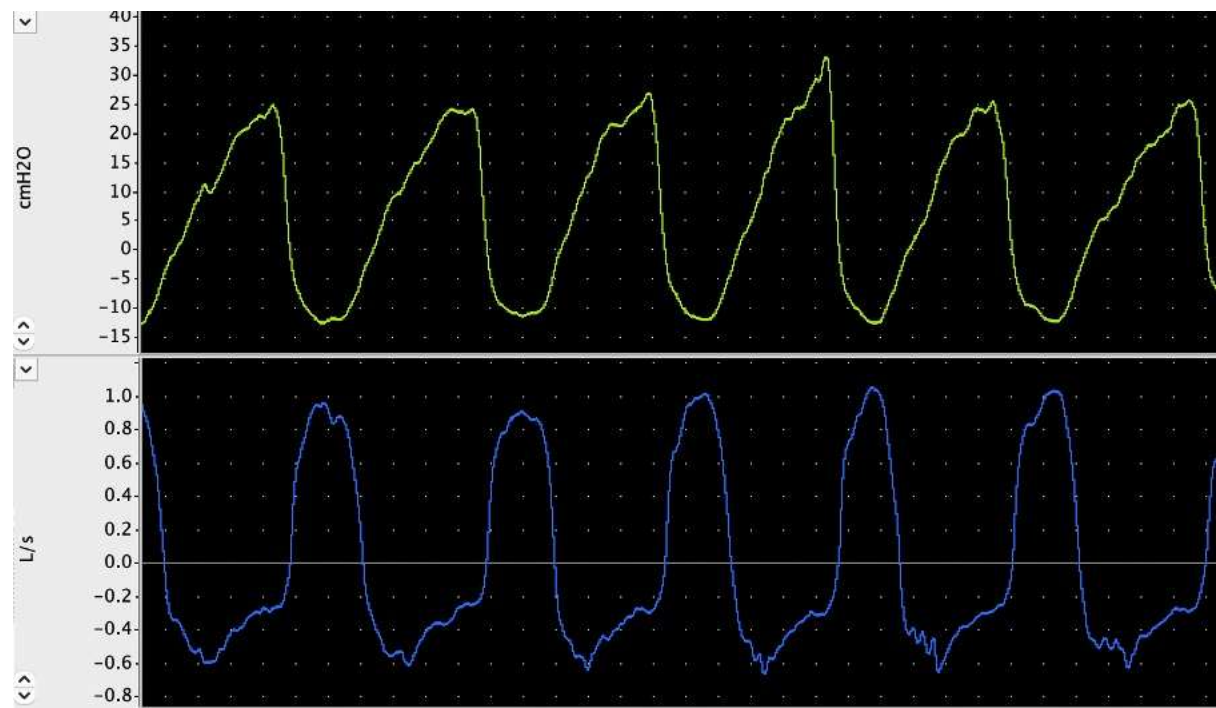


Figure 4

